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L4 9 L3 AND HUMANIZED

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L5 9 DUP REMOVE L4 (0 DUPLICATES REMOVED)

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L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS
2002:594705 Document No. 137:139366 Immunoregulatory **antibodies** and uses thereof. Hariharan, Kandasamy; Hanna, Nabil (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002060485 A2 20020808, 103 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,

ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2621 20020131. PRIORITY: US 2001-772938 20010131; US 2001-855717 20010516; US 2001-985646 20011105; US 2001-PV331187 20011109.

AB A combination **antibody** therapy for treating B cell malignancies using an immunoregulatory **antibody**, esp. an anti-B7, anti-**CD23**, or anti-CD40L **antibody**, and a B-cell depleting **antibody**, esp. anti-CD19, anti-CD20, anti-CD22 or anti-CD37 **antibody**, is provided. Preferably, the combination therapy will comprise anti-B7 and anti-CD20 **antibody** administration. IDEC-131, IDEC-114, and Rituxan monoclonal **antibodies** are of special interest.

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS

2002:594704 Document No. 137:153822 **CD23** antagonistic **antibodies** for treatment of neoplastic disorders. Hariharan, Kandasamy; Hanna, Nabil; Braslawsky, Gary R.; Pathan, Nuzhat (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002060484 A1 20020808, 88 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2620 20020131. PRIORITY: US 2001-772938 20010131; US 2001-855717 20010516; US 2001-985646 20011105.

AB Methods and kits for the treatment of neoplastic disorders comprising the use of a **CD23** antagonist are provided. These **CD23** antagonists are monoclonal, polyclonal, **chimeric**, **humanized** or primatized **antibodies**, e.g. IDEC-152. The **CD23** antagonist may be used alone or in combination with radiotherapeutic or chemotherapeutic agents. In particularly preferred embodiments the **CD23** antagonists may be used to treat B cell chronic lymphocytic leukemia (B-CLL).

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS

2002:220424 Document No. 136:246408 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS

2002:833304 Document No. 137:309495 Use of **CD23** antagonists for the treatment of neoplastic disorders. Hariharan, Kandasamy; Hanna,

Nabil; Braslawsky, Gary; Pathan, Nuzhat (USA). U.S. Pat. Appl. Publ. US 2002159996 A1 20021031, 42 pp., Cont.-in-part of U.S. Ser. No. 772,938. (English). CODEN: USXXCO. APPLICATION: US 2001-985646 20011105. PRIORITY: US 2001-772938 20010131.

AB Methods and kits for the treatment of neoplastic disorders comprising the use of a **CD23** antagonist are provided. The **CD23** antagonist may be used alone or in combination with chemotherapeutic agents. In particularly preferred embodiments the **CD23** antagonists may be used to treat B cell chronic lymphocytic leukemia (B-CLL). The **CD23** antagonists are anti-**CD23** **antibodies**, particularly IDEC 152. IDEC 152 synergizes with chemotherapeutic agents in inducing apoptosis of cancer cells.

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS

2002:773675 Document No. 137:293559 Human Fc.epsilon.RII receptor homolog. Wood, William I.; Goddard, Audrey; Gurney, Austin; Yuan, Jean; Baker, Kevin P.; Chen, Jian (Genentech, Inc., USA). Eur. Pat. Appl. EP 1247817 A2 20021009, 37 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL. (English). CODEN: EPXXDW. APPLICATION: EP 2002-12909 19990308. PRIORITY: US 1998-PV84637 19980507; EP 1999-912321 19990308.

AB The authors disclose the cloning and recombinant expression of a protein (PRO792) which exhibits extracellular domain homol. to human **CD23** .

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS

2000:861519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Deboer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2000072879 A1 20001207, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.

AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors (UgE Fc receptor type I and **CD23**), expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and **chimeric** mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS

1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, **humanized** IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of

1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:30:38 ON 23 APR 2003
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L2 3300 S L1 AND CD23
L3 90 S L2 AND CHIMERIC
L4 9 S L3 AND HUMANIZED
L5 9 DUP REMOVE L4 (0 DUPLICATES REMOVED)

=> s l3 and binding affinity
L6 0 L3 AND BINDING AFFINITY

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L7 6 L2 AND BINDING AFFINITY

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PROCESSING COMPLETED FOR L7
L8 6 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-6 cbib abs

L8 ANSWER 1 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2002416734 EMBASE Vaccination for birch pollen allergy: Induction of affinity-matured or blocking IgG **antibodies** does not account for the reduced binding of IgE to Bet v 1. Svenson M.; Jacobi H.H.; Bodtger U.; Poulsen L.K.; Rieneck K.; Bendtzen K.. K. Bendtzen, Institute for Inflammation Research, Rigshospitalet University Hospital, Blegdamsvej 9, Copenhagen DK-2100, Denmark. kben@mail.dk. Molecular Immunology 39/10 (603-612) 2003.
Refs: 52.
ISSN: 0161-5890. CODEN: IMCHAZ.
Publisher Ident.: S 0161-5890(02)00198-0. Pub. Country: United Kingdom.
Language: English. Summary Language: English.
AB Specific allergy vaccination (SAV) is associated with increased levels of allergen specific IgG in serum. It is not clear, however, to what extent qualitative changes in allergen binding to IgG may be induced as well. We therefore analyzed the binding of the major allergen in pollen of birch (Betula verrucosa) (Bet v 1), the major allergen in birch pollen, to serum IgG and IgE, separately and in competition. Sera from six birch pollen-allergic patients were obtained before and after 5 years of SAV, and binding was assessed with (125)I-Bet v 1. Before SAV, IgG bound more than eight times the amount of Bet v 1 compared with IgE, and together they accounted for more than 85% of the serum binding capacity. While SAV induced minimal changes in IgE binding, the IgG binding capacities increased 6-32 times. In contrast, the binding avidities (K(d) 28-40pM) changed less than 20%, pre- and post-SAV IgG provided similar inhibition of Bet v 1 binding to IgE at equimolar levels, and cross inhibition studies between IgG and IgE showed low inter-individual differences. Following SAV, all sera reduced Bet v 1 binding to **CD23**(+) cells, correlating with reduced binding of Bet v 1 to IgE ($P<0.001$). These results show that high avidity IgG of low inter-individual difference in Bet v 1 binding quality is the dominant binding factor of Bet v 1 in sera of birch pollen-allergic patients, and that SAV-induced inhibition of binding of Bet v 1 to IgE can be explained mainly or solely by increased amounts of IgG.

L8 ANSWER 2 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2000042846 EMBASE A polymorphic CD40 ligand (CD154) molecule mediates CD40-dependent signalling but interferes with the ability of soluble CD40 to functionally block CD154:CD40 interactions. Barnhart B.; Ford G.S.; Bhushan A.; Song C.; Covey L.R.. Dr. L.R. Covey, Dept. of Cell Biol. and Neuroscience, Nelson Biological Laboratories, State University of New Jersey, 604 Allison Road, Piscataway, NJ 08854, United States. Immunology 99/1 (54-61) 2000.
Refs: 30.
ISSN: 0019-2805. CODEN: IMMUAM. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB We report the characterization of a naturally occurring polymorphism in CD40 ligand (CD40L, CD154) expressed by activated T cells from a young female patient. This polymorphism encodes a nonconservative Gly .fwdarw. Arg substitution in amino acid 219 in the extracellular, CD40 binding

domain of the molecule. Studies carried out with 293 epithelial cells ectopically expressing the polymorphic protein (CD154/G219R) revealed reduced levels of binding to different anti-CD154 monoclonal **antibodies** (mAb) and CD40-immunoglobulin (CD40-Ig). However, recognition of the polymorphic and wild-type CD154 molecules by a polyclonal antiserum was comparable, suggesting that the polymorphism affects the ability of the protein to interact with CD40 but does not significantly alter its surface expression. To determine if reduced cross-linking of CD40 mediated decreased functional effects, three CD40-dependent properties were measured. We found that pathways leading to the induction of surface **CD23**, CD80, and I.gamma. transcription were activated in response to CD154/G219R signalling. However, the decrease in affinity for CD40 by the mutated CD 154 affected the ability of CD40-Ig to efficiently interfere with the binding and effectively block induced CD80 expression. In contrast, we found that the 5c8 mAb, which recognized the polymorphic molecule to a similar extent as wild-type CD154, effectively blocked the interaction between CD154/G219R and CD40 as measured by CD80 expression. These findings suggest that naturally occurring polymorphisms in the CD 154 molecule may affect the ability of CD40-mediated functions to be blocked by soluble CD40 or anti-CD154 Mab in the therapeutic treatment of disease and graft rejection.

L8 ANSWER 3 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

1999313189 EMBASE Upregulation of Fc.epsilon.RI on human basophils by IgE **antibody** is mediated by interaction of IgE with Fc.epsilon.RI.

MacGlashan D. Jr.; Lichtenstein L.M.; McKenzie-White J.; Chichester K.; Henry A.J.; Sutton B.J.; Gould H.J.. Dr. D. MacGlashan Jr., Johns Hopkins Asthma/Allergy Center, 5501 Hopkins Bayview Circle, Baltimore, MD 21224, United States. Journal of Allergy and Clinical Immunology 104/2 I (492-498) 1999.

Refs: 29.

ISSN: 0091-6749. CODEN: JACIBY. Pub. Country: United States. Language: English. Summary Language: English.

AB Background: IgE is now known to upregulate the expression of Fc.epsilon.RI on human basophils. It is not known which receptor on basophils mediates this process of upregulation. Objective: We sought to determine whether galectin- 3, Fc.ovrhdot.RII (**CD23**), or Fc.epsilon.RI were involved in the upregulation of Fc.epsilon.RI by IgE. Methods: The role of galectin-3 was examined by measuring the influence of .alpha.-lactose on upregulation. Basophils were examined for expression of Fc.epsilon.RII (**CD23**) by flow cytometry and messenger (m)RNA expression. Functional discrimination between binding to Fc.epsilon.RII or Fc.epsilon.RI was examined through the use of mutant IgE-Fc fragments or anti-Fc.epsilon.RII **antibody**. Results: Upregulation of Fc.epsilon.RI on basophils in the presence of IgE was not altered by coincubation with .alpha.-lactose, eliminating a role for galectin-3. Basophils were not found to express Fc.epsilon.RII, as determined by flow cytometry with enriched basophil preparations or RT-PCR with highly purified basophil preparations. A mutant of the Fc fragment of IgE (IgE-Fc), which binds to Fc.epsilon.RI with a greater than 10-fold lower affinity than IgE or wild-type IgE- Fc but exhibits no change in affinity for Fc.epsilon.RII, allowed us to distinguish between the functions of the two Fc receptors. The mutant (R334S; Henry et al 1997) was required at about 30-fold higher concentration than the wild-type IgE-Fc for the same stimulation of Fc.epsilon.RI expression on basophils, thus excluding a role for Fc.epsilon.RII in the response. In addition, treatment of basophils with anti-Fc.epsilon.RII **antibody** (MHM6), which is known to be competitive with IgE, had no effect on the expression of Fc.epsilon.RI or the ability of IgE to upregulate expression of Fc.epsilon.RI. Conclusion: Collectively, these data indicate that IgE interacts with Fc.epsilon.RI to upregulate its expression on human basophils.

L8 ANSWER 4 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
1999134306 EMBASE Binding of anti-**CD23** monoclonal **antibody** to the leucine zipper motif of Fc.epsilon.RII/**CD23** on B cell membrane promotes its proteolytic cleavage: Evidence for an effect on the oligomer/monomer equilibrium. Munoz O.; Brignone C.; Grenier-Brossette N.; Bonnefoy J.-Y.; Cousin J.-L.. J.-L. Cousin, INSERM U343, Hopital de l'Archet, BP 79, F-06202 Nice Cedex 03, France. cousin@unice.fr. Journal of Biological Chemistry 273/48 (31795-31800) 27 Nov 1999.
Refs: 54.
ISSN: 0021-9258. CODEN: JBCHA3. Pub. Country: United States. Language: English. Summary Language: English.

AB In the present study we have compared the binding of two monoclonal **antibodies** to **CD23**, EBVCS1 and mAb25, which recognize the stalk and the lectin domain, respectively, on the **CD23** molecule. At 4.degree.C, EBVCS1 binds to about 10% of the receptors recognized by mAb25 on the B cell surface. At 37.degree.C, whereas mAb25 reaches its maximal binding within a few seconds, EBVCS1 requires 60 min to bind to the same extent. Stabilization of the oligomeric structure of **CD23** with IgE strongly affects in a dose-dependent fashion the number of binding sites seen by EBVCS1 but not the t(1/2) to reach them, suggesting that EBVCS1 binds to the coiled coil region through an allosteric mechanism. EBVCS1 rapidly down-modulates the membrane **CD23** expression with a coincident increase of **CD23** -soluble fragments in the culture medium, an effect that is inhibited by IgE. In contrast, mAb25, as well as IgE, protects **CD23** from proteolytic cleavage and stimulates its endocytosis. These results suggest that EBVCS1 unravels the coiled coil structure of **CD23**, rendering it more susceptible to pro, teolytic attack. This supports the oligomeric model proposed previously (Gould, H., Sutton, B., Edmeades, R., and Beavil, A. (1991) Monogr. Allergy 29, 28-49). The biological significance of these observations is discussed.

L8 ANSWER 5 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
1998331237 EMBASE STAT6, NF-.kappa.B and C/EBP in **CD23** expression and IgE production. Tinnell S.B.; Jacobs-Helber S.M.; Sterneck E.; Sawyer S.T.; Conrad D.H.. Dr. D.H. Conrad, MCV Station, PO Box 980678, Richmond, VA 23298, United States. International Immunology 10/10 (1529-1538) 1998.
Refs: 69.
ISSN: 0953-8178. CODEN: INIMEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB STAT6, NF-.kappa.B (p50) and C/EBP.beta. transcription factors (TF) were examined with respect to **CD23** regulation. Electrophoretic mobility shift assay (EMSA), competition and supershift analysis demonstrated that STAT6 binds the CD23a promoter but with a lower affinity than the consensus site. STAT6(-/-) mice were analyzed for **CD23** levels and showed reduced expression after CD40 ligand trimer (CD40LT) stimulation. However, normal **CD23** expression and even some IgE production was induced in STAT6(-/-) mice with CD40LT/IL-4. EMSA analysis indicated that the CD23a STAT site was bound by a protein in nuclear extracts from CD40 .+-. IL-4-stimulated STAT6(-/-) B cells. Western blot analysis of these nuclear extracts demonstrated the presence of STAT3 and STAT5, suggesting that these STATs can induce **CD23** in this situation. Further supporting evidence was obtained by showing that IL-2 and IL-4 both synergize with CD40 in an identical manner for **CD23** induction on STAT6(-/-) B cells. EMSA analysis of the two putative NF-.kappa.B sites confirmed binding to both, although one site bound with a higher affinity than the second. Analysis of p50(-/-) mice indicated that this subunit was not necessary for **CD23** induction or CD40/IL-4-induced IgE production. Finally, no role for C/EBP was observed in **CD23** induction by EMSA or by **CD23** induction analysis in C/EBP.beta.(-/-) mice, whereas the absence of C/EBP.beta. did have an effect on IgE production and lipopolysaccharide-induced B cell

proliferation. Based on these data, a model is presented which suggests that **CD23** superinduction results from STAT and NF-.kappa.B interaction.

L8 ANSWER 6 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
93162132 EMBASE Document No.: 1993162132. Identification of a distinct low-affinity receptor for human interleukin- 4 on pre-B cells. Fanslow W.C.; Spriggs M.K.; Rauch C.T.; Clifford K.N.; Macduff B.M.; Ziegler S.F.; Schooley K.A.; Mohler K.M.; March C.J.; Armitage R.J.. Immunex Research/Development Corp, 51 University St,Seattle, WA 98101, United States. Blood 81/11 (2998-3005) 1993.
ISSN: 0006-4971. CODEN: BLOOAW. Pub. Country: United States. Language: English. Summary Language: English.
AB Biotinylated interleukin-4 (IL-4) was used to examine IL-4 receptor (IL-4R) expression on a range of human B-cell lines by flow cytometry. Using high concentrations of biotinylated IL-4, we have identified a novel low-affinity IL-4 receptor expressed at high levels on pre-B lines. Expression of this low-affinity receptor did not correlate with detected mRNA levels for the previously cloned receptor or with reactivity of two anti-human IL-4R monoclonal **antibodies** (MoAb). Radiolabeled IL-4 cross-linking studies using pre-B lines showed a doublet of 65 to 75 Kd in contrast to the 110- to 130- Kd molecule detected on cells expressing the cloned IL-4R. A soluble IL-4 binding protein (IL-4bp) was purified from the supernatants of three pre-B lines expressing the low-affinity receptor on their surface. IL-4bp could block both IL-4-mediated **CD23** induction on tonsil B cells and IL-4-induced inhibition of proliferation of the pre-B line JM1. Partial N-terminal amino acid sequence was obtained from purified IL-4bp that confirmed this protein to be novel. A 12 amino acid peptide based on the IL-4bp sequence was used to produce a polyclonal antiserum that was reactive with purified IL-4bp, and also bound to the surface of pre-B cells but not to murine CTLL cells transfected with the human IL-4R. Blocking MoAb against the previously characterized high-affinity receptor inhibited IL-4-mediated proliferation of hIL-4R+ CTLL cells but had no effect on IL-4-induced inhibition of JM1 cell proliferation, and only partially inhibited IL-4-mediated **CD23** and sIgM induction and proliferation of tonsil B cells. The data presented here provide evidence for a novel cell-surface expressed low-affinity IL-4R that also exists as a biologically active soluble IL-4 binding protein.

```
=> s antibody binding affinity
L9          218 ANTIBODY BINDING AFFINITY

=> s l9 and anti-CD23
L10           0 L9 AND ANTI-CD23

=> s l9 and CD23
L11           0 L9 AND CD23

=> s l9 and Fc epsilon receptor II
L12           0 L9 AND FC EPSILON RECEPTOR II

=> s l9 and "RSSKSLLYKDGKTYLN"
L13           0 L9 AND "RSSKSLLYKDGKTYLN"

=> s l9 and "1x109 Ka per M"
L14           0 L9 AND "1X109 KA PER M"

=> d his

     (FILE 'HOME' ENTERED AT 10:30:16 ON 23 APR 2003)
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     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:30:38 ON
     23 APR 2003
L1      2419928 S ANTIBODY
L2         3300 S L1 AND CD23
L3           90 S L2 AND CHIMERIC
L4            9 S L3 AND HUMANIZED
L5            9 DUP REMOVE L4 (0 DUPLICATES REMOVED)
L6            0 S L3 AND BINDING AFFINITY
L7            6 S L2 AND BINDING AFFINITY
L8            6 DUP REMOVE L7 (0 DUPLICATES REMOVED)
L9          218 S ANTIBODY BINDING AFFINITY
L10           0 S L9 AND ANTI-CD23
L11           0 S L9 AND CD23
L12           0 S L9 AND FC EPSILON RECEPTOR II
L13           0 S L9 AND "RSSKSLLYKDGKTYLN"
L14           0 S L9 AND "1X109 KA PER M"

=> s l2 and biocore assays
L15           0 L2 AND BIOCORE ASSAYS

=> s l2 and biacore assay
L16           0 L2 AND BIACORE ASSAY

=> dup remove l9
PROCESSING COMPLETED FOR L9
L17         111 DUP REMOVE L9 (107 DUPLICATES REMOVED)

=> s l17 and CD23 antibody
L18           0 L17 AND CD23 ANTIBODY

=> s l2 and antagonist
L19          88 L2 AND ANTAGONIST

=> dup remove l19
PROCESSING COMPLETED FOR L19
L20           59 DUP REMOVE L19 (29 DUPLICATES REMOVED)

=> d l20 1-59 cbib abs

L20  ANSWER 1 OF 59  CAPLUS  COPYRIGHT 2003 ACS
2002:594704   Document No. 137:153822  CD23 antagonistic
     antibodies for treatment of neoplastic disorders.  Hariharan,
     Kandasamy; Hanna, Nabil; Braslawsky, Gary R.; Pathan, Nuzhat (Idec
     Pharmaceuticals Corporation, USA).  PCT Int. Appl. WO 2002060484 A1
     20020808, 88 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA,
     BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
     ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
     KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
     OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
     UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM;
     RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB,
     GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).
     CODEN: PIXXD2.  APPLICATION: WO 2002-US2620 20020131.  PRIORITY: US
     2001-772938 20010131; US 2001-855717 20010516; US 2001-985646 20011105.
AB   Methods and kits for the treatment of neoplastic disorders comprising the
     use of a CD23 antagonist are provided.  These
     CD23 antagonists are monoclonal, polyclonal, chimeric,
     humanized or primatized antibodies, e.g. IDEC-152.  The
     CD23 antagonist may be used alone or in combination with
     radiotherapeutic or chemotherapeutic agents.  In particularly preferred
     embodiments the CD23 antagonists may be used to treat
     B cell chronic lymphocytic leukemia (B-CLL).
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L20 ANSWER 2 OF 59 CAPLUS COPYRIGHT 2003 ACS
2002:833304 Document No. 137:309495 Use of **CD23 antagonists** for the treatment of neoplastic disorders. Hariharan, Kandasamy; Hanna, Nabil; Braslawsky, Gary; Pathan, Nuzhat (USA). U.S. Pat. Appl. Publ. US 2002159996 A1 20021031, 42 pp., Cont.-in-part of U.S. Ser. No. 772,938. (English). CODEN: USXXCO. APPLICATION: US 2001-985646 20011105. PRIORITY: US 2001-772938 20010131.

AB Methods and kits for the treatment of neoplastic disorders comprising the use of a **CD23 antagonist** are provided. The **CD23 antagonist** may be used alone or in combination with chemotherapeutic agents. In particularly preferred embodiments the **CD23 antagonists** may be used to treat B cell chronic lymphocytic leukemia (B-CLL). The **CD23 antagonists** are anti-**CD23 antibodies**, particularly IDEC 152. IDEC 152 synergizes with chemotherapeutic agents in inducing apoptosis of cancer cells.

L20 ANSWER 3 OF 59 MEDLINE
2002620047 Document Number: 22254868. PubMed ID: 12161424. p38 Mitogen-activated protein kinase regulates interleukin-4-induced gene expression by stimulating STAT6-mediated transcription. Pesu Marko; Aittomaki Saara; Takaluoma Kati; Lagerstedt Anssi; Silvennoinen Olli. (Institute of Medical Technology, University of Tampere, FIN-33014 Tampere, Finland.) JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Oct 11) 277 (41) 38254-61. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB STAT6 functions as a critical mediator of IL-4-stimulated gene activation, and the function of STAT6 is regulated by both tyrosine and serine kinase activities. Here we analyzed the role of serine phosphorylation in regulation of STAT6-mediated transcription. Optimal transcriptional response of IL-4-inducible promoters requires costimulatory signals through CD40-stimulated intracellular kinases such as p38 MAPK. We found that the p38 MAPK inhibitor SB202190 as well as the dominant negative p38 MAPK inhibited interleukin (IL)-4 regulated expression of **CD23** in Ramos B cells. IL-4 stimulation did not stimulate p38 MAPK activity, but inhibition of p38 MAPK activity directly correlated with inhibition of IL-4-induced gene activation. Dissection of individual response elements on IL-4-regulated promoter showed that C/EBP beta-mediated transcription was insensitive to SB202190 treatment in B cells whereas STAT6-mediated transcription was regulated by p38 MAPK. The IL-4-induced immediate activation events of STAT6 were not affected by p38 MAPK activity. Furthermore, phosphoamino acid analysis and phosphopeptide mapping indicated that STAT6 is not a direct substrate for p38 MAPK. Instead, p38 MAPK was found to directly regulate the activity of the transactivation domain of STAT6. These results show that, in addition to the well established proinflammatory effects, p38 MAPK also provides a costimulatory signal for IL-4-induced gene responses by directly stimulating the transcriptional activation of STAT6.

L20 ANSWER 4 OF 59 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 1
2003009034 EMBASE Extracellular adenosine 5'-triphosphate induces a loss of **CD23** from human dendritic cells via activation of P2X(7) receptors. Sluyter R.; Wiley J.S.. R. Sluyter, Department of Medicine, University of Sydney, Nepean Hospital, Level 5 South Block, Penrith, NSW 2750, Australia. rons@med.usyd.edu.au. International Immunology 14/12 (1415-1421) 1 Dec 2002.
Refs: 39.
ISSN: 0953-8178. CODEN: INIMEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Dendritic cells (DC) express a number of P2X receptors including the P2X(7)/P2Z receptor whose activation by extracellular adenosine 5'-triphosphate (ATP) induces the influx of calcium, DC maturation, cytokine release and apoptosis. In B lymphocytes ATP induces the rapid

shedding of **CD23** and CD62 ligand by activating a membrane metalloprotease. In this study, we examined the expression and early effects of P2X(7) receptor activation on monocyte-derived DC, generated from individuals either wild-type or homozygous for a loss-of-function single nucleotide polymorphism at position 1513 of the P2X7 gene. Labeling with an anti-human P2X(7) receptor mAb demonstrated that DC express the P2X(7) receptor at a lower level than macrophages. Short-term incubations (5 min) of DC with ATP induced an influx of ethidium(+) (314 Da) into wild-type DC, but not into DC homozygous for the loss-of-function polymorphism. In contrast to results with ethidium(+), ATP did not induce the influx of the viability dye propidium(2+) (415 Da) into DC in short-term incubations. Addition of ATP also induced a rapid loss of **CD23** from the surface of wild-type DC (t(1/2) < 120 s), and this loss was inhibited by oxidized ATP and KN-62 which are known P2X(7) receptor **antagonists**. Moreover, ATP-induced shedding of **CD23** was slower from DC homozygous for the loss-of-function polymorphism than from wild-type DC. The data show that monocyte-derived DC express the P2X(7) receptor whose activation opens a cation-selective channel, and which leads to rapid and near complete shedding of **CD23**. Both of these functions of the P2X(7) receptor are impaired on DC from subjects who are homozygous for the loss-of-function 1513 polymorphism.

L20 ANSWER 5 OF 59 MEDLINE

2002247531 Document Number: 21982556. PubMed ID: 11986939. Production of matrix metalloproteinase-9 in early stage B-CLL: suppression by interferons. Bauvois B; Dumont J; Mathiot C; Kolb J-P. (Unite 365 INSERM, Section de Recherche, Institut Curie, Pavillon Pasteur, 26 rue d'Ulm, 75248 Paris cedex 05, France.) LEUKEMIA, (2002 May) 16 (5) 791-8. Journal code: 8704895. ISSN: 0887-6924. Pub. country: England: United Kingdom. Language: English.

AB Besides vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), matrix metalloproteinases (MMPs) play critical roles in angiogenesis, tumor invasion and metastasis. Increased angiogenesis is observed in chronic B lymphocytic leukemia (B-CLL) and published data reported VEGF and bFGF production in this disease. The purpose of this study was to investigate MMP expression in early stage B-CLL. Elevated MMP-9 concentrations were detected by ELISA in the sera of B-CLL patients (median level 250 ng/ml) compared with healthy donors (67 ng/ml) (P < 0.0001), and immunostaining with **antibodies** against MMP-9 and B cell antigens (CD19, **CD23**) substantiated the presence of MMP-9 in tumoral B lymphocytes. By using RT-PCR, ELISA and zymography experiments, we confirmed that B-CLL cells expressed and released the pro-form of MMP-9 with Mr 92 kDa (158-1300 pg/ml/10(6) cells/48 h), p-aminophenylmercuric acetate generating a 82 kDa active form. In contrast, the production of MMP-9 by normal counterpart B cells was significantly low (28-169 pg/ml/10(6)cells/48 h). Moreover, B-CLL culture supernatants contained bFGF (median levels 17 pg/ml/10(6) cells/48 h), VEGF (1.4 pg/ml/10(6) cells/48 h) and TNF-alpha (0.2 pg/ml/10(6) cells/48 h). TNF-alpha and VEGF **antibodies** blocked MMP-9 at the mRNA and protein levels. Interferons (IFNs) type I or type II repressed MMP-9 gelatinolytic activity in a dose and time dependency, and this was reflected by a parallel inhibition of MMP-9 mRNA and protein. IFNs however did not affect the production of bFGF, VEGF and TNF-alpha. Together, our data show that B-CLL lymphocytes synthesize MMP-9 and emphasize the specific inhibitory actions of IFNs on its expression.

L20 ANSWER 6 OF 59 MEDLINE

2001341620 Document Number: 21240390. PubMed ID: 11342414. Ligation of CD11b and CD11c beta(2) integrins by **antibodies** or soluble **CD23** induces macrophage inflammatory protein 1alpha (MIP-1alpha) and MIP-1beta production in primary human monocytes through a pathway dependent on nuclear factor-kappaB. Rezzonico R; Imbert V; Chicheportiche

R; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine, University Hospital, Geneva, Switzerland.. rezzonic@unice.fr) . BLOOD, (2001 May 15) 97 (10) 2932-40. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB Chemokines and adhesion molecules such as integrins play a major part in the trafficking, extravasation, and recruitment of leukocytes to inflammatory sites. This study investigated the effects of beta(2) integrin engagement on chemokine production by freshly isolated human monocytes. We found that ligation of CD11b or CD11c but not CD11a alpha chains of beta(2) integrins by **antibodies** or soluble **CD23** (sCD23) fusion proteins rapidly induced transcription and secretion of interleukin 8, macrophage inflammatory protein (MIP) 1alpha, and MIP-1beta. Because the promoters of these chemokine genes contain kappaB binding sites, we assessed the possible role of nuclear factor-kappaB (NF-kappaB) in controlling induction of the genes through beta(2) integrin engagement. Electrophoretic mobility shift assays showed that sCD23 or **antibodies** to CD11b or to CD11c up-regulated DNA-binding activity of NF-kappaB. Activation of NF-kappaB was accompanied by degradation of its cytosolic inhibitor IkappaB-alpha. Blockade of depletion of IkappaB-alpha by proteasome inhibitors (proteasome inhibitor I or acetyl-leucinyl-leucinyl-norleucinal) led to concomitant inhibition of NF-kappaB DNA-binding activity and expression of MIP-1alpha and MIP-1beta messenger RNA induced by beta(2) integrin ligation. These results suggest that triggering of CD11b or CD11c beta(2) integrin on primary human monocytes provides activation signals leading to nuclear translocation of NF-kappaB and subsequent secretion of MIP-1alpha and MIP-1beta that may have an important role in recruitment of other inflammatory cells during initiation of an inflammatory response.

L20 ANSWER 7 OF 59 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

2001410508 EMBASE Autopsy case of lymphoplasmacytic lymphoma with a large submucosal tumor in the stomach. Okada Y.; Mori H.; Maeda T.; Ito Y.; Hasegawa M.; Kageyama T.. Dr. Y. Okada, Department of Pathology, Osaka Medical College, 2-7 Daigaku-machi, Takatsuki, Osaka 569-8686, Japan. yokada@art.osaka-med.ac.jp. Pathology International 51/10 (802-806) 2001.

Refs: 24.

ISSN: 1320-5463. CODEN: PITEES. Pub. Country: Japan. Language: English. Summary Language: English.

AB An autopsy case of lymphoplasmacytic lymphoma with a large submucosal tumor in the stomach is presented. The patient was a 77-year-old woman with gastric lymphoma associated with Waldenstrom's macroglobulinemia of IgM-.lambda. type. Diagnosis was initially mucosa-associated lymphoid tissue (MALT) lymphoma of the stomach, because gastric biopsy specimens showed epitheliotropic proliferation (lymphoepithelial lesion) of the lymphoma cells. Post-mortem examination revealed a large gastric lymphoma with metastatic foci in the esophagus, larynx, trachea, lungs, spleen and lymph nodes. The bone marrow was also involved. Lymphoma cells consisted of small lymphocytoid cells occasionally admixed with blast-like large cells and a large number of plasmacytoid or plasma cells. Centrocyte-like cells were not found. Lymphoepithelial lesions were not conspicuous in autopsy specimens. Immunohistochemically, lymphoma cells reacted with CD20, CD45, CD79a, anti-IgM, anti-.lambda. protein and anti-BCL-2, but not with CD5, CD10, **CD23** or CD38. Based on these findings, the revised diagnosis of the present case was lymphoplasmacytic lymphoma, and it highlighted the differential diagnostic problem from marginal zone B-cell lymphoma of MALT type.

L20 ANSWER 8 OF 59 MEDLINE

2001209686 Document Number: 21195373. PubMed ID: 11298826.

Metalloprotease inhibitor-mediated inhibition of mouse immunoglobulin production. Kilmon M A; Mayer R J; Marshall L A; Conrad D H. (Virginia

Commonwealth University, Department of Microbiology and Immunology, Richmond, VA 23298, USA.. mkilmon@hsc.vcu.edu) . IMMUNOLOGY, (2001 Mar) 102 (3) 281-8. Journal code: 0374672. ISSN: 0019-2805. Pub. country: England: United Kingdom. Language: English.

AB High levels of membrane **CD23** have been shown to decrease immunoglobulin E (IgE). **CD23** is a very labile molecule and is cleaved from the cell surface by an unknown metalloprotease. Two metalloprotease inhibitors, compound A (N-[4-hydoxyamino-2-(R)-isobutyl-3-(S)propargylthiomethylsuccinyl]-(S)-phenylalnine-N'-methyl-amide) and compound B (N-[3-(S)-hydroxy-4-hydroxyamino-2-(R)-(2-naphthylmethyl) succinyl]-(S)-tert-leucinamide), were chosen for their ability to inhibit human **CD23** cleavage and selectively inhibit IgE production. The ability of these inhibitors to block cleavage of murine **CD23** and immunoglobulin production in an in vitro system was examined. The inhibitors blocked sCD23 release from B cells. The inhibitors also decreased IgE production by B cells; however, 20-30 times more inhibitor was needed to give a similar amount of inhibition as compared with sCD23 release. The effects on immunoglobulin production did not require the presence of **CD23** in that these inhibitors also blocked in vitro immunoglobulin production when B cells from **CD23**-/- mice were used. The inhibitors decreased production of all other immunoglobulin isotypes examined and reduced the number of IgE **antibody**-forming cells (AFC) while having no effect on cell proliferation or viability. The level of Iepsilon transcripts in cells treated with compounds A and B were not different as compared with control cells. These results suggest that while these inhibitors effectively inhibit IgE production in a **CD23**-specific manner in the human, these compounds, in the mouse, inhibit immunoglobulin production by an unknown mechanism that is unrelated to **CD23**.

L20 ANSWER 9 OF 59 CAPLUS COPYRIGHT 2003 ACS

2001:361001 Document No. 136:52380 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31(New Drugs for Asthma, Allergy and COPD), 182-185 (English) 2001. CODEN: PRRRAE. ISSN: 1422-2140. Publisher: S. Karger AG.

AB A review. In addn. to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such mols. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen mols., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific mols. in the inflammatory cascade is currently being addressed with "humanized" monoclonal **antibodies** and sol. receptors/receptor **antagonists**, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface mols. such as **CD23**.

L20 ANSWER 10 OF 59 SCISEARCH COPYRIGHT 2003 ISI (R)

2001:404948 The Genuine Article (R) Number: 431CQ. Anti-interleukin-1 therapy in rheumatic diseases. Dayer J M (Reprint); Feige U; Edwards C K; Burger D. Univ Hosp Geneva, Div Immunol & Allergy, CH-1211 Geneva 14, Switzerland (Reprint); Amgen Inc, Dept Pharmacol, Thousand Oaks, CA 91320 USA; Amgen Inc, Dept Inflammat Res, Thousand Oaks, CA 91320 USA. CURRENT OPINION IN RHEUMATOLOGY (MAY 2001) Vol. 13, No. 3, pp. 170-176. Publisher: LIPPINCOTT

WILLIAMS & WILKINS. 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA. ISSN: 1040-8711. Pub. country: Switzerland; USA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Recent research has shown that in the processes of rheumatoid arthritis (RA), interleukin (IL)-1 is one of the pivotal cytokines in initiating disease, and the body's natural response, IL-1 receptor **antagonist** (IL-1 Ra), has been shown conclusively to block its effects. In laboratory and animal studies inhibition of IL-1 by either **antibodies** to IL-1 or IL-1 Ra proved beneficial to the outcome. To date, two large well-controlled studies in patients with RA led to the conclusion that IL-1 Ra is clinically effective and that it slows progression of bone damage as measured radiographically. Being a specific, selective inhibitor of the IL-1 pathway, IL-1 Ra could constitute an important new approach to treating patients with RA that significantly reduces the signs and symptoms of the disease, reduces joint destruction and up to now has proved Safe and well tolerated. (C) 2001 Lippincott Williams & Wilkins, Inc.

L20 ANSWER 11 OF 59 CAPLUS COPYRIGHT 2003 ACS

2000:861519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE **antagonists**. Deboer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2000072879 A1 20001207, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.

AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE **antagonists** by inhibiting the binding of IgE mols. to IgE receptors (UgE Fc receptor type I and **CD23**), expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L20 ANSWER 12 OF 59 CAPLUS COPYRIGHT 2003 ACS

2000:133697 Document No. 132:203144 Low-adenosine antisense oligonucleotide agents, compositions, kits and treatments for respiratory disorders. Nyce, Jonathan W. (East Carolina University, USA). PCT Int. Appl. WO 2000009525 A2 20000224, 1343 pp. DESIGNATED STATES: W: AU, CA, CN, MX, RU, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US17712 19990803. PRIORITY: US 1998-95212 19980803.

AB A compn. comprises a nucleic acid comprising an oligo antisense to a target such as polypeptide(s) assocd. with an ailment afflicting lung airways, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents. The agent of the invention may be prepd. by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more antisense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low

T content, and by optionally replacing A in the antisense oligonucleotides with a universal base. The agent, compn. and formulations are used for prophylactic, preventive and therapeutic treatment of ailments assocd. with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), ischemic conditions including ischemia itself, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, pancreatic cancer, lung cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastasis, etc., as well as all types of cancers with may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including radiation, chemotherapy, **antibody** therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs. The invention is exemplified with specificity and pharmacokinetic studies using phosphorothioated antisense oligonucleotides targeted to the adenosine receptors A1, A2a, A2b, and A3.

L20 ANSWER 13 OF 59 MEDLINE

2000225227 Document Number: 20225227. PubMed ID: 10764157. Expression of a functional inducible nitric oxide synthase in hairy cell leukaemia and ESKOL cell line. Roman V; Zhao H; Fourneau J M; Marconi A; Dugas N; Dugas B; Sigaux F; Kolb J P. (INSERM U365, Institut Curie, Paris, France.) LEUKEMIA, (2000 Apr) 14 (4) 696-705. Journal code: 8704895. ISSN: 0887-6924. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The expression of nitric oxide synthase (NOS) isoforms was investigated in the established ESKOL hairy cell line and in leukemic cells of patients with hairy cell leukemia (HCL). By reverse transcription-polymerase chain reaction (RT-PCR), these cells were found to spontaneously express inducible NOS (iNOS)-specific mRNA, but not endothelial constitutive NOS (ecNOS) mRNA. The iNOS protein was detected by immunofluorescence in the cytoplasm of permeabilized leukemic cells and ESKOL cells, using different anti-iNOS monoclonal **antibodies**. A protein of 135 kDa was identified by Western blotting in ESKOL and HCL lysates, confirming the presence of an iNOS in these cells. Cytosolic homogenates displayed NOS catalytic activity, as measured by the conversion of 14C-labelled L-arginine into 14C L-citrulline and by detection in situ using the DAF-2DA (diaminofluorescein diacetate) NO-sensitive fluorescent probe. Ligation of **CD23** (low affinity IgE receptor) was found to increase iNOS expression in ESKOL and conversely to decrease the percentage of cells undergoing apoptosis, as measured by the percentage of cells expressing annexin V. These results indicate that, as in chronic B cell lymphocytic leukemia cells (B-CLL) a functional iNOS is expressed constitutively in hairy cells that contributes to protecting these tumoral cells from apoptosis.

L20 ANSWER 14 OF 59 MEDLINE

1999282971 Document Number: 99282971. PubMed ID: 10352303. Mechanisms of IL-10 production in human microglia-T cell interaction. Chabot S; Williams G; Hamilton M; Sutherland G; Yong V W. (Department of Oncology, University of Calgary, Alberta, Canada.) JOURNAL OF IMMUNOLOGY, (1999 Jun 1) 162 (11) 6819-28. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB IL-10, a cytokine with important anti-inflammatory properties, is

generated within the CNS during neuroinflammation. The mechanism for its production is poorly understood. Since infiltrating lymphocytes come into close proximity with the macrophage-like cells of the CNS, the microglia, we have used an in vitro human microglia-T cell coculture system to address the mechanisms of IL-10 production. We demonstrate that microglia or activated T cells alone secrete negligible amounts of IL-10, but that their coculture results in significant IL-10 production, which was effected by both cell types. IL-10 generation was cell contact dependent, and treatment with anti-CD40, CTLA-4-Fc, or anti-**CD23** decreased the IL-10 content in microglia-T cell cocultures. The combination of anti-CD40 and CTLA-4-Fc reduced IL-10 levels to the negligible amounts seen with T cells or microglia in isolation. By also measuring TNF-alpha levels, specificity of cytokine regulation was observed; while anti-CD40 and CTLA-4-Fc reduced IL-10 and TNF-alpha levels, anti-**CD23** did not affect TNF-alpha while attenuating IL-10 generation. Anti-very late Ag-4, which decreased TNF-alpha levels, did not affect IL-10. These results implicate the CD40, B7, and **CD23** pathways in IL-10 production following microglia-T cell encounter and have relevance to the regulation of an anti-inflammatory response within the CNS.

L20 ANSWER 15 OF 59 MEDLINE DUPLICATE 2

1999135997 Document Number: 99135997. PubMed ID: 9949321. Production of chemokines and proinflammatory and antiinflammatory cytokines by human alveolar macrophages activated by IgE receptors. Gosset P; Tillie-Leblond I; Oudin S; Parmentier O; Wallaert B; Joseph M; Tonnel A B. (Unite INSERM U416, Institut Pasteur, Lille, France.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1999 Feb) 103 (2 Pt 1) 289-97. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: The alveolar macrophage (AM) expresses the low affinity IgE receptor and has the ability to produce not only several proinflammatory cytokines (TNF-alpha, IL-1, IL-6) but also antiinflammatory cytokines (IL-1 receptor **antagonist** [IL-1ra], IL-10), chemokines (IL-8, monocyte chemotactic protein-1 [MCP-1]), and macrophage inflammatory protein-1alpha (MIP-1alpha). OBJECTIVE: The aim of this study was to evaluate the capacity of the AM from patients with allergic asthma and control subjects to produce chemokines and antiinflammatory versus proinflammatory cytokines after activation by IgE receptors and to define the role of **CD23** in this activation. METHODS: AMs were collected by bronchoalveolar lavage from 13 patients with allergic asthma and 14 healthy subjects. Adherent AMs were activated either by the successive addition of IgE and anti-IgE or by monoclonal mouse IgG anti-**CD23** or by a control monoclonal mouse **antibody**. TNF, IL-1beta, IL-1ra, IL-10, IL-8, MCP-1, and MIP-1alpha levels were evaluated in supernatants of AMs incubated for 18 hours and in some cases after 4 hours of incubation. RESULTS: Activation by IgE and anti-IgE **antibodies** significantly increased the production of TNF, IL-1beta, IL-8, MCP-1, MIP-1alpha, and IL-10 in both control subjects and patients with asthma, whereas the increase for IL-1ra was only significant for the control subjects. Whereas F(ab) fragments of anti-**CD23** **antibodies** inhibited IgE plus anti-IgE-induced cytokine production, activation by monoclonal IgG anti-**CD23** **antibodies** reproduced the effect of IgE immune complexes. At 4 hours, the secretion of proinflammatory cytokines was increased by activation by IgE receptors, in contrast to antiinflammatory cytokines. In addition, analysis of the balance between proinflammatory and antiinflammatory cytokines showed that IgE-dependent activation largely favored the proinflammatory cytokines, particularly in patients with asthma. CONCLUSION: IgE-dependent activation by the FcepsilonRII receptor upregulates the synthesis of both chemokines and antiinflammatory cytokines in addition to proinflammatory cytokines. However, AMs from patients with allergic asthma may promote airway inflammation after activation by IgE receptors through its preferential effect on proinflammatory cytokines.

L20 ANSWER 16 OF 59 MEDLINE
1999279845 Document Number: 99279845. PubMed ID: 10353405. Up-regulation of interleukin-4 and **CD23**/FcepsilonRII in minimal change nephrotic syndrome. Cho B S; Yoon S R; Jang J Y; Pyun K H; Lee C E. (Department of Pediatrics, College of Medicine, Kyung Hee University, Seoul, Korea.) PEDIATRIC NEPHROLOGY, (1999 Apr) 13 (3) 199-204. Journal code: 8708728. ISSN: 0931-041X. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Although the pathogenesis of childhood minimal change nephrotic syndrome (MCNS) has not been clearly defined, the current hypothesis favors an involvement of T cell dysfunction. The symptom onset and the relapse of MCNS are frequently associated with allergy and increased IgE levels in sera. Since a T cell-derived cytokine interleukin-4 (IL-4) plays a key role in the regulation of IgE production and allergic response, we investigated the role of IL-4 in the pathophysiology of MCNS. Using fluorescence-activated cell scanning we observed a significantly higher expression of **CD23**, the type II IgE receptor (FcepsilonRII), on fresh B cells from active MCNS patients (n=22) compared with age-matched healthy normal controls (n=12). The upregulation of **CD23** correlates with greater IL-4 activity in the culture supernatant of MCNS peripheral blood lymphocytes (PBLs) than normal PBLs stimulated by mitogens, as assessed by the **CD23**-inducing effect of the PBL supernatant on tonsillar B cells. Furthermore, Northern blot and reverse transcription-based polymerase chain reaction analysis have revealed significantly elevated levels of IL-4 mRNAs both in mitogen-stimulated and unstimulated MCNS PBLs, compared with healthy normals or disease controls with other renal disorders. Together these results strongly suggest that the upregulation of IL-4 in T cells may be part of the T cell dysfunction involved in MCNS.

L20 ANSWER 17 OF 59 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
1999071483 EMBASE Antagonistic effects of an alternative splice variant of human IL-4, IL- 4.delta.2, on IL-4 activities in human monocytes and B cells. Arinobu Y.; Atamas S.P.; Otsuka T.; Niiro H.; Yamaoka K.; Mitsuyasu H.; Niho Y.; Hamasaki N.; White B.; Izuhara K.. Y. Arinobu, Department of Clinical Chemistry, Laboratory Medicine, Kyushu University, Fukuoka 812-8582, Japan. Cellular Immunology 191/2 (161-167) 1 Feb 1999. Refs: 44.
ISSN: 0008-8749. CODEN: CLIMB8. Pub. Country: United States. Language: English. Summary Language: English.

AB IL-4 is a pleiotropic cytokine which exerts its actions on various lineages of hematopoietic and nonhematopoietic cells. This cytokine is one of the central regulators of immunity in health and disease states. An alternative splice variant, in which the second of four exons is omitted, has been recently described and designated as IL-4.delta.2. The variant has been previously described as a potential naturally occurring **antagonist** of human IL-4 (hIL-4)-stimulated T cell proliferation. In this study, we investigated the effects of recombinant human (rh) IL-4.delta.2 on monocytes and B cells. In monocytes, rhIL-4.delta.2 blocked inhibitory action of hIL-4 on LPS-induced cyclooxygenase-2 expression and subsequent prostaglandin E2 secretion. In B cells, rhIL-4.delta.2 was an **antagonist** of the hIL-4-induced synthesis of IgE and expression of **CD23**. Our results broaden the spectrum of hIL-4-antagonistic activities of rhIL-4.delta.2, thus creating the background for the potential use of rhIL-4.delta.2 as a therapeutic anti-hIL-4 agent.

L20 ANSWER 18 OF 59 MEDLINE
1999110801 Document Number: 99110801. PubMed ID: 9893200. IL-4 and IgE-anti-IgE modulation of 15(S)-hydroxyeicosatetraenoic acid release by mononuclear phagocytes. Profita M; Vignola A M; Mirabella A; Siena L; Sala A; Gjomarkaj M; Bousquet J; Bonsignore G. (Istituto di Fisiopatologia

Respiratoria, C.N.R., Palermo, Italy.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1999 Jan) 103 (1 Pt 1) 159-64. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: IL-4 modulates the synthesis of IgE, the expression of **CD23**, and the release of 15(S)-hydroxyeicosatetraenoic (15[S]-HETE). OBJECTIVE: We evaluated the release of 15(S)-HETE by IL-4-stimulated monocytes and verified whether the observed increase in 15(S)-HETE release after passive sensitization and anti-IgE challenge of IL-4-treated monocytes was secondary to an increased **CD23** expression. METHODS: Human monocytes were incubated for 24, 48, and 72 hours with IL-4 (10 ng/mL) with or without an IgE-anti-IgE stimulation. We evaluated **CD23** expression by immunocytochemistry and 15(S)-HETE release by HPLC and RIA. To prove that the increase in 15(S)-HETE release was due to the effect of IL-4 on **CD23**, we performed experiments with an anti-**CD23** blocking mAb. RESULTS: **CD23** expression and 15(S)-HETE release were significantly increased by IL-4, reaching a peak after 72 hours ($P < .02$). After passive sensitization with human IgE and anti-IgE challenge, IL-4-stimulated monocytes released higher amounts of 15(S)-HETE than IL-4-unstimulated monocytes ($P < .02$). Pretreatment with the anti-human B-cell **CD23** MHM6 mAb caused a dose-dependent inhibition of 15(S)-HETE release. CONCLUSIONS: This study shows that immunologic challenge of IL-4-treated, passively sensitized monocytes results in a **CD23**-dependent additional increase of 15(S)-HETE release, indicating the presence of a synergistic effect of IL-4 on **CD23** expression and 15(S)-HETE production.

L20 ANSWER 19 OF 59 MEDLINE

1999087797 Document Number: 99087797. PubMed ID: 9870911. **CD23** and allergic pulmonary inflammation: potential role as an inhibitor. Cernadas M; De Sanctis G T; Krinzman S J; Mark D A; Donovan C E; Listman J A; Kobzik L; Kikutani H; Christiani D C; Perkins D L; Finn P W. (Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.) AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY, (1999 Jan) 20 (1) 1-8. Journal code: 8917225. ISSN: 1044-1549. Pub. country: United States. Language: English.

AB **CD23**, a receptor for immunoglobulin E, is expressed at increased levels in asthmatic and atopic individuals and has been associated with disorders characterized by chronic inflammation. Using an established murine model, we employed several complementary strategies to investigate the role of **CD23** in allergic pulmonary inflammation and airway hyperresponsiveness (AHR). Specifically, these approaches included the modulation of **CD23** function in vivo by administration of anti-**CD23** monoclonal **antibody** (mAb) or Fab fragments to wild-type mice and the analysis of **CD23**-deficient mice. Administration of anti-**CD23** mAb, but not anti-**CD23** Fab fragments, produced attenuation of pulmonary inflammation, AHR, and CD8(+) T-cell activation. On the basis of a model that the anti-**CD23** mAb transduces, whereas the Fab fragment inhibits, **CD23** signaling, these results suggest that **CD23** negatively regulates pulmonary inflammation and AHR. This hypothesis is supported by our observation that **CD23**-deficient mice developed increased inflammation and AHR after sensitization and challenge with allergen. Together, these results indicate that **CD23** negatively regulates pulmonary inflammation and airway hyperreactivity.

L20 ANSWER 20 OF 59 MEDLINE

1999049828 Document Number: 99049828. PubMed ID: 9834082. Inhibitors of the p38 mitogen-activated kinase modulate IL-4 induction of low affinity IgE receptor (**CD23**) in human monocytes. Marshall L A; Hansbury M J; Bolognese B J; Gum R J; Young P R; Mayer R J. (Department of Immunopharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, USA.) JOURNAL OF IMMUNOLOGY, (1998 Dec 1) 161 (11) 6005-13.

Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB **CD23**, the low affinity IgE receptor, is up-regulated on the surface of IL-4-treated B cells and monocytes and is immediately proteolytically processed, releasing soluble fragments of **CD23**. Here, we report that inhibitors of the p38 mitogen-activated kinase (p38 MAPK), SK&F 86002 or the more selective inhibitor, SB 203580, reduce the levels of soluble **CD23** formed by IL-4-stimulated human monocytes or the human monocytic cell line, U937. In contrast to compounds such as the metalloprotease inhibitor batimastat ([4-(N-hydroxyamino)-2-(R)-isobutyl-3-(S)-(2-thiophenethiomethyl)s uccinyl]-(S)-phenylalanine-N-methylamide, sodium salt), p38 MAPK inhibitors do not directly inhibit proteolytic processing of **CD23**. Further, evaluation of surface intact **CD23** (iCD23) by flow cytometry demonstrated that SK&F 86002 and SB 203580 reduced the surface expression of iCD23 in a concentration-dependent fashion, while batimastat increased the surface expression of iCD23. The decrease in surface iCD23 was accompanied by a decrease in total cell-associated **CD23** protein levels but not **CD23** mRNA. IL-4 induced a late (>4-h) increase in p38 MAPK activity and corresponding activation of its substrate MAPKAPK-2. This activation was blocked by addition of SB 203580 before IL-4 induction, in parallel with the inhibition of **CD23** expression. Modulation of **CD23** by **antibodies** has been shown to alleviate the symptoms of murine collagen-induced arthritis, implicating **CD23** as an important proinflammatory agent. These data show that in addition to the known cytokine inhibitory actions of SK&F 86002 and SB 203580, they also confer an additional potential anti-inflammatory activity through modulation of **CD23** expression.

L20 ANSWER 21 OF 59 SCISEARCH COPYRIGHT 2003 ISI (R)

1998:746134 The Genuine Article (R) Number: 122GY. Specific antagonism of type I IL-4 receptor with a mutated form of murine IL-4. Schnare M; Blum H; Juttner S; Rollinghoff M; Gessner A (Reprint). INST KLIN MIKROBIOL & IMMUNOL, POB 3540-65174, D-91054 ERLANGEN, GERMANY (Reprint); UNIV ERLANGEN NURNBERG, INST KLIN MIKROBIOL IMMUNOL & HYG, D-8520 ERLANGEN, GERMANY. JOURNAL OF IMMUNOLOGY (1 OCT 1998) Vol. 161, No. 7, pp. 3484-3492 . Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: GERMANY. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB IL-4 is a pleiotropic cytokine that is essential for the differentiation of Th2 cells and is critically involved in the pathogenesis of certain infectious and allergic diseases, We have produced and functionally characterized a mutant of murine IL-4 (IL-4.Y119D) as a potential **antagonist** of IL-4. The analysis of IL-4R binding revealed no differences between wild-type and mutated IL-4. Despite this finding, IL-4.Y119D was unable to induce proliferation of several IL-4-responsive T cell lines mediated via the type I IL-JR (IL-4R alpha/common gamma chain (gamma c chain)) and specifically inhibited the proliferative effect of wild-type IL-4. In contrast, with IL-4.Y119D we found induction of MHC class II and **CD23** molecules on resting splenic B cells as well as proliferation of B9 plasmocytoma cells. In addition, IL-4.Y119D induced mRNA for soluble IL-JR, leading to the release of soluble IL-4R protein by spleen cells. In macrophages, mutated IL-4 in combination with IFN-gamma induced TNF-alpha-dependent killing of Leishmania major parasites such as wild-type IL-4, The agonistic effects of IL-4.Y119D were observed on cells expressing the IL-13R alpha-chain, including an IL-13R cu-chain transfected T cell line, but were absent in T cells that lack this molecule, indicating that IL-4.Y119D conveys its activity via the type II IL-4R (IL-4R alpha/IL-13R alpha). The described IL-4 mutant, therefore, represents a new tool to use in dissecting different IL-4 functions that are mediated by either type I or type II IL-4R complexes.

L20 ANSWER 22 OF 59 MEDLINE
1998343944 Document Number: 98343944. PubMed ID: 9677315. **CD23** (FcepsilonRII) release from cell membranes is mediated by a membrane-bound metalloprotease. Marolewski A E; Buckle D R; Christie G; Earnshaw D L; Flamberg P L; Marshall L A; Smith D G; Mayer R J. (SmithKline Beecham Pharmaceuticals, Upper Merion, 709 Swedeland Road, King of Prussia, PA 19406, USA.) BIOCHEMICAL JOURNAL, (1998 Aug 1) 333 (Pt 3) 573-9. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **CD23** (low-affinity IgE receptor, FcepsilonRII) is expressed as a Type II extracellular protein on a variety of cells such as B-cells, monocytes and macrophages and is cleaved from the cell surface to generate several distinct fragments. The expression of **CD23** on the cell surface as well as the generation of soluble fragments of **CD23** has been shown to be involved in the regulation of IgE synthesis. Here we report that the release of **CD23** from the cell surface is mediated by a metalloprotease. An assay utilizing purified **CD23** and an neo-epitope **antibody** specific for one of the known cleavage products is described and used to demonstrate unambiguously the cleavage of **CD23** by a distinct protease. Characterization of the mechanism of **CD23** processing shows that the protease exists as an integral membrane protein with a functional molecular mass of approx. 63 kDa as determined by gel-filtration chromatography. The **CD23**-cleaving activity found in enriched plasma membranes from RPMI 8866 cells is inhibited by the metalloprotease inhibitors 1, 10-phenanthroline and imidazole and by the matrix metalloprotease inhibitor batimastat, but not by inhibitors of cysteine proteases, serine proteases or acid proteases. The same or a similar activity that cleaves **CD23** to the known 33 kDa fragment and is inhibited by batimastat is present in diverse cell types such as unstimulated fibroblasts and monocytic cell lines not expressing **CD23**, as well as in the Epstein-Barr virus-transformed B-cell line, RPMI 8866, which constitutively expresses **CD23**.

L20 ANSWER 23 OF 59 MEDLINE
1998209738 Document Number: 98209738. PubMed ID: 9550368. Induction of IL-10 synthesis by human keratinocytes through **CD23** ligation: a cyclic adenosine 3',5'-monophosphate-dependent mechanism. Becherel P A; LeGoff L; Frances C; Chosidow O; Guillosson J J; Debre P; Mossalayi M D; Arock M. (Department of Immunology, Pitie-Salpetriere Hospital, Paris, France.) JOURNAL OF IMMUNOLOGY, (1997 Dec 15) 159 (12) 5761-5. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Ligation of the low affinity receptor for IgE, **CD23**/Fc epsilonRII, in human keratinocytes (HK) and monocytes induces the synthesis of proinflammatory cytokines (IL-6 and TNF-alpha), partly under the dependence of cAMP and nitric oxide pathways. Moreover, **CD23** ligation induces IL-10 production in human monocytes. Since synthesis of IL-10 by HK is still a matter of debate, we investigate whether keratinocytes could produce IL-10 upon **CD23** stimulation. Here, our data show that **CD23** ligation induces significant IL-10 synthesis in HK, a phenomenon inhibited by cAMP **antagonists**, but not by inhibitors of the nitric oxide pathway. Accordingly, cAMP agonist induced significant IL-10 synthesis by HK, while nitric oxide-releasing chemical did not. Treatment of HK with anti-IL-10 mAb potentiated their **CD23**-mediated TNF-alpha synthesis. These data indicate that engagement of surface **CD23** on human keratinocytes induces the synthesis of IL-10, which, in turn, down-regulates their proinflammatory response.

L20 ANSWER 24 OF 59 MEDLINE
1998018268 Document Number: 98018268. PubMed ID: 9378995. Modulation of antigen-induced B and T cell responses by antigen-specific IgE

antibodies. Oshiba A; Hamelmann E; Haczku A; Takeda K; Conrad D H; Kikutani H; Gelfand E W. (Department of Pediatrics, National Jewish Medical and Research Center, Denver, CO 80206, USA.) JOURNAL OF IMMUNOLOGY, (1997 Oct 15) 159 (8) 4056-63. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Ag-specific IgE Abs not only mediate immediate hypersensitivity through mast cell activation, but also enhance in vitro Ag presentation and in vivo specific Ab responses in mice. To delineate the role of IgE Ab in the modulation of Ag-specific responses, spleen cells from OVA-sensitized BALB/C mice were cultured together with OVA-specific IgE (or IgG isotypes). OVA-dependent proliferative responses and anti-OVA IgE production were enhanced in the presence of anti-OVA IgE. A significant decrease in IFN-gamma secretion in OVA-stimulated cultures was observed in the presence of anti-OVA IgE, but no changes in IL-4 production were detected. Anti-OVA IgG isotypes or anti-TNP IgE showed no significant effect on any of these Ag-dependent responses. Addition of anti-**CD23** Ab abolished these effects of anti-OVA IgE. Further, OVA-sensitized spleen cells from **CD23**-deficient mice responded to in vitro stimulation with OVA, but demonstrated no modulation by anti-OVA IgE. These results demonstrate that Ag-specific IgE not only augments Ag presentation and T cell proliferation, but also alters the pattern of cytokine production and increases specific IgE synthesis. These modulatory effects of Ag-specific IgE appear to be mediated by binding to Fc epsilon RII/**CD23**.

L20 ANSWER 25 OF 59 MEDLINE

1998012856 Document Number: 98012856. PubMed ID: 9349841. Low glutamine concentrations induce phenotypical and functional differentiation of U937 myelomonocytic cells. Spittler A; Oehler R; Goetzinger P; Holzer S; Reissner C M; Leutmezer F; Rath V; Wrba F; Fuegger R; Boltz-Nitulescu G; Roth E. (Department of Surgery, Research Laboratories, University of Vienna, 1090 Vienna, Austria.) JOURNAL OF NUTRITION, (1997 Nov) 127 (11) 2151-7. Journal code: 0404243. ISSN: 0022-3166. Pub. country: United States. Language: English.

AB L-Glutamine is the most abundant free amino acid of the human body and is essential for the culture of many cell types. Clinically, reduction of glutamine by administration of glutaminase or the use of glutamine analogs is a common therapy for patients with acute lymphocytic leukemia. In the current study, we investigated the influence of glutamine concentrations on the human myelomonocytic cell line U937. Decreasing the glutamine concentration evoked a reduction in DNA synthesis ($R2 = 0.9885$, $P < 0.0001$), increased cell volume ($P < 0.01$) and the cytoplasm/nuclear ratio, and enhanced the development of vacuoles but did not influence cell viability. Culturing cells in reduced concentrations of glutamine augmented the percentage of cells expressing CD64 (Fc receptor for IgG/FcgammaRI, $P < 0.01$), CD11b (complement receptor type 3/CR3, $P < 0.001$) and CD71 (transferrin receptor, $P < 0.05$). The percentage of U937 cells expressing **CD23** (low affinity receptor for IgE/FcepsilonRII) was increased at low concentrations of glutamine at both the protein ($P < 0.01$) and mRNA levels. The percentage of U937 cells phagocytizing opsonized E. coli ($P < 0.001$) or latex particles ($P < 0.001$) was enhanced by lowering the glutamine concentration. In conclusion, reducing glutamine concentration causes differentiation of the cell line U937 along the monocytic pathway. These effects may indicate a mechanistic basis for prior published evidence that glutaminase and glutamine **antagonists** are effective anti-tumor agents.

L20 ANSWER 26 OF 59 MEDLINE

1998101492 Document Number: 98101492. PubMed ID: 9440542. A thiol antioxidant regulates IgE isotype switching by inhibiting activation of nuclear factor-kappaB. Yanagihara Y; Basaki Y; Kajiwara K; Ikizawa K. (Clinical Research Center for Allergy, National Sagamihara Hospital, Sagamihara City, Kanagawa, Japan.) JOURNAL OF ALLERGY AND CLINICAL

IMMUNOLOGY, (1997 Dec) 100 (6 Pt 2) S33-8. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB The binding site for nuclear factor-kappaB (NF-kappaB) is present at the promoter region of the germline Cepsilon gene, but there is little information on whether this factor is involved in regulating IgE synthesis by human B cells. Accordingly, we studied the role of NF-kappaB in germline Cepsilon transcription by using two human Burkitt's lymphoma B cell lines, DND39 and DG75. In both cell lines, n-acetyl-L-cysteine (NAC), a potent thiol antioxidant, inhibited the triggering of the nuclear expression of NF-kappaB by IL-4 and by anti-CD40 monoclonal **antibody**. Although IL-4 activated signal transducers and activators of transcription (STAT) 6 in addition to NF-kappaB, NAC treatment or the transfection of decoy oligodeoxynucleotides for NF-kappaB or STAT6 only partly blocked IL-4-induced germline Cepsilon transcription. However, these two decoy oligodeoxynucleotides together almost completely abrogated IL-4-induced germline Cepsilon transcription. Of note, CD40-mediated enhancement of IL-4-driven germline Cepsilon transcription was markedly decreased by NAC or by a decoy oligodeoxynucleotide for NF-kappaB. The effect of NAC was also examined on deletional switch recombination underlying the isotype switch to IgE. NAC inhibited the generation of Smu/Sepsilon switch fragments in normal human B cells costimulated with IL-4 and anti-CD40 monoclonal **antibody**. It also abolished IL-4-induced upregulation of CD40 but promoted upregulation of **CD23**. These results suggest that coordination of NF-kappaB and STAT6 may be required for induction of germline Cepsilon transcription by IL-4, and that CD40-mediated NF-kappaB activation may be important in regulating both enhancement of germline Cepsilon transcription and class switching to IgE.

L20 ANSWER 27 OF 59 MEDLINE DUPLICATE 3

97008118 Document Number: 97008118. PubMed ID: 8855294. Prostaglandin E2 receptors of the EP2 and EP4 subtypes regulate activation and differentiation of mouse B lymphocytes to IgE-secreting cells. Fedyk E R; Phipps R P. (Department of Microbiology, University of Rochester School of Medicine and Dentistry, NY 14642, USA.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Oct 1) 93 (20) 10978-83. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Prostaglandin E2 (PGE2) is a potent lipid molecule with complex proinflammatory and immunoregulatory properties. PGE2 can shape the immune response by stimulating the production of IgE **antibody** by B lymphocytes and the synthesis of T-helper type 2 cytokines [e.g., interleukin (IL)-4, IL-10], while inhibiting production of Th1 cytokines (e.g., interferon-gamma, IL-12). It is unknown what type of receptor binds PGE2 and modulates these responses. Recent analyses in nonhematopoietic cells have identified six PGE2 receptors (EP1, EP2, EP3 alpha, EP3 beta, EP3 gamma, and EP4). This investigation examines quiescent B lymphocytes and reports that these cells express mRNA encoding EP1, EP2, EP3 beta, and EP4 receptors. The immunoregulatory functions of each receptor were investigated using small molecule agonists that preferentially bind EP receptor subtypes. Unlike agonists for EP1 and EP3, agonists that bound EP2 or EP2 and EP4 receptors strongly inhibited expression of class II major histocompatibility complex and **CD23** and blocked enlargement of mouse B lymphocytes stimulated with IL-4 and/or lipopolysaccharide. PGE2 promotes differentiation and synergistically enhances IL-4 and lipopolysaccharide-driven B-cell immunoglobulin class switching to IgE. Agonists that bound EP2 or EP2 and EP4 receptors also strongly stimulated class switching to IgE. Experiments employing inhibitors of cAMP metabolism demonstrate that the mechanism by which EP2 and EP4 receptors regulate B lymphocyte activity requires elevation of cAMP. In conclusion, these data suggest that **antagonists** to EP2 and EP4 receptors will be important for diminishing allergic and IgE-mediated asthmatic responses.

L20 ANSWER 28 OF 59 MEDLINE

96238065 Document Number: 96238065. PubMed ID: 8647169. Soluble CD40 ligand induces expression of CD25 and **CD23** in resting human tonsillar B lymphocytes. Burlinson E L; Graber P; Bonnefoy J Y; Ozanne B W; Cushley W. (Division of Biochemistry and Molecular Biology, Institute of Biomedical and Life Sciences, University of Glasgow, Scotland.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 May) 26 (5) 1069-73. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB In this report, we describe the dose-dependent increase in both CD25 and **CD23** levels on resting human B cells in response to CD40 ligation, as mediated by soluble CD40 ligand (sCD40L) or anti-CD40 **antibody** . In combination with interleukin (IL)-4, sCD40L had limited additive effects on CD25 expression, but significantly enhanced **CD23** expression on tonsillar B cells. Interferon-gamma (IFN-gamma) exerted no inhibitory effect upon increases in CD25 or **CD23** driven by CD40 ligation with sCD40L or anti-CD40 **antibody**. These data suggest that the induction of CD25 and **CD23** genes by IL-4 is mediated, at least in part, by an IFN-gamma-sensitive component, whereas gene activation driven via CD40 ligation involves signaling pathways which are not sensitive to IFN-gamma.

L20 ANSWER 29 OF 59 MEDLINE

96151984 Document Number: 96151984. PubMed ID: 8562926. Interleukin-13 inhibits interleukin-2-induced proliferation and protects chronic lymphocytic leukemia B cells from in vitro apoptosis. Chaouchi N; Wallon C; Goujard C; Tertian G; Rudent A; Caput D; Ferrera P; Minty A; Vazquez A; Delfraissy J F. (Laboratoire Virus Neurone et Immunite, Faculte de Medecine Paris Sud, France.) BLOOD, (1996 Feb 1) 87 (3) 1022-9. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB Human interleukin-13 (IL-13) acts at different stages of the normal B-cell maturation pathway with a spectrum of biologic activities overlapping those of IL-4. B chronic lymphocytic leukemia (B-CLL) is characterized by the accumulation of slow-dividing and long-lived monoclonal B cells, arrested at the intermediate stage of their differentiation. In vitro, B-CLL cells exhibit a spontaneous apoptosis regulated by different cytokines. In this report, we show that IL-13 (10 to 200 ng/mL) acts directly on monoclonal B-CLL cells from 12 patients. (1) IL-13 enhances **CD23** expression and induces soluble **CD23** secretion by B-CLL cells but does not exhibit a growth factor activity. (2) IL-13 inhibits IL-2 responsiveness of B-CLL cells, activated either with IL-2 alone or through crosslinking of Igs or ligation of CD40 antigen. (3) IL-13 protects B-CLL cells from in vitro spontaneous apoptosis. The effects of IL-13 on neoplasic B cells were slightly less than those of IL-4 and occurred independently of the presence of IL-4. The present observations show that IL-13 may exhibit a negative regulatory effect on neoplasic B cells in contrast with that observed in normal B cells, and suggest that IL-13 could be an important factor in the pathogenesis of CLL by preventing the death of monoclonal B cells. Moreover, B-CLL may be an interesting model to study the regulation of the expression of IL-13 receptor and/or signal transduction pathways.

L20 ANSWER 30 OF 59 MEDLINE DUPLICATE 4

97093003 Document Number: 97093003. PubMed ID: 8938565. Immunomodulatory and hematopoietic effects of recombinant human interleukin-6 in patients with advanced renal cell cancer. Schuler M; Peschel C; Schneller F; Fichtner J; Farber L; Huber C; Aulitzky W E. (Department of Medicine III, Johannes Gutenberg University, Mainz, Germany.) JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, (1996 Nov) 16 (11) 903-10. Journal code: 9507088. ISSN: 1079-9907. Pub. country: United States. Language: English.

AB Interleukin-6 (IL-6) is a cytokine with pleiotropic biologic activities on

B cells, T cells, and hematopoietic progenitors. The present study was undertaken to assess pharmacodynamic effects of subcutaneous administration of IL-6 on blood counts, immunologic parameters, and acute-phase reactants. Blood samples were taken from patients with advanced renal cell cancer participating in a phase II trial of recombinant human IL-6. Multiparameter FACS analyses of peripheral blood mononuclear cells were performed using **antibodies** against CD3, CD4, CD8, HLA-DR, CD56, CD28, CD38, CD19, sIgM, and sIgG. Serum levels of IL-10, soluble **CD23** (sCD23), sCD25, IL-1 receptor **antagonist** protein (IL-1RA), soluble tumor necrosis factor (TNF) receptors (sTNF-R) p55 and p75, and soluble IL-6 receptor (sIL-6R) were detected by ELISA systems. Levels of C-reactive protein (CRP), neopterin, fibrinogen, beta 2-microglobulin, and immunoglobulins M, G, and A were measured by standard methods. In response to administration of IL-6, a significant increment in platelet counts was observed, reaching peak levels after 21 days of treatment. In contrast, leukocyte subsets remained unaffected. No change in number of immunophenotype of peripheral blood B cells, T cells, or natural killer cells could be detected following IL-6 administration. Blood levels of sCD23, IL-10, sIL-6R, neopterin, beta 2-microglobulin, and immunoglobulin subsets were not influenced by cytokine therapy. However, administration of IL-6 led to a slow increment of acute-phase reactants CRP and fibrinogen. Furthermore, the anti-inflammatory molecules sTNF-R p55 and p75 were induced by IL-6, whereas serum levels of IL-1RA remained unchanged. Finally, an increase in blood levels of sCD25 was observed. In conclusion, IL-6 in vivo predominantly acts as a regulator of inflammation and a megakaryocyte differentiation factor.

L20 ANSWER 31 OF 59 MEDLINE

96152742 Document Number: 96152742. PubMed ID: 8566063. Nerve growth-factor and anti-CD40 provide opposite signals for the production of IgE in interleukin-4-treated lymphocytes. Brodie C; Oshiba A; Renz H; Bradley K; Gelfand E W. (Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206, USA.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jan) 26 (1) 171-8. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Nerve growth factor (NGF) is a well-known neurotrophic factor acting on both the peripheral and the central nervous systems. In addition, it has been shown to play a role in the function of the immune system through specific receptors. Both high-affinity and low-affinity NGF receptors (NGFR) are expressed on human B lymphocytes. The low-affinity NGFR has been shown to have structural homology with another specific B cell surface molecule, CD40, which plays an important role in IgE production. In view of the structural similarities of the p75 NGFR and CD40 we examined whether NGF may also be involved in the regulation of IgE production. We found that NGF and anti-CD40 exerted opposite effects on the induction of IgE by IL-4 in peripheral blood mononuclear cells. NGF inhibited the induction of IgE by IL-4 and this inhibition was not mediated through blocking of the induction of **CD23** nor through inhibition of IL-4R expression. The inhibition of IL-4-dependent IgE production was observed on surface (s)IgE+ and sIgE-/sIgM+ B lymphocytes. Anti-CD40 on the other hand, exerted an enhancing effect on IgE production and its addition to IL-4 provided a signal that was resistant to the inhibitory effect of NGF. Antagonistic effects of NGF and IL-4 were also observed for other Ig isotypes since IL-4 prevented the increase in IgA and IgM production induced by NGF. These data indicate that although NGFR and CD40 belong to the same receptor superfamily and exert similar proliferative effects on B lymphocytes, they interact differently with IL-4 in the regulation of IgE production.

L20 ANSWER 32 OF 59 CAPLUS COPYRIGHT 2003 ACS

1995:789548 Document No. 123:196599 IgE **antagonists** for treatment

of parasitic infection. Amiri, Payman; Haak-Fredscho, Mary; Jardieu, Paula M. (Genentech, Inc., USA). PCT Int. Appl. WO 9519181 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US87 19950105. PRIORITY: US 1994-184083 19940118.

AB This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE **antagonist**. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE **antagonist** also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

L20 ANSWER 33 OF 59 MEDLINE

95372367 Document Number: 95372367. PubMed ID: 7544003. The killing of Leishmania major by human macrophages is mediated by nitric oxide induced after ligation of the Fc epsilon RII/**CD23** surface antigen. Vouldoukis I; Riveros-Moreno V; Dugas B; Ouaaz F; Becherel P; Debre P; Moncada S; Mossalayi M D. (Centre National de la Recherche Scientifique, Pitie-Salpetriere Hospital, Paris, France.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Aug 15) 92 (17) 7804-8. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Serum IgE concentrations and the expression of the low-affinity receptor for IgE (Fc epsilon RII/**CD23**) are increased in cutaneous leishmaniasis or after immune challenge with Leishmania antigens. In vitro, the ligation of **CD23** by IgE-anti-IgE immune complexes (IgE-IC) or by anti-**CD23** monoclonal **antibody** (mAb) induces nitric oxide (NO) synthase and the generation of various cytokines by human monocytes/macrophages. The present study shows that IgE-IC, via **CD23** binding, induce intracellular killing of Leishmania major in human monocyte-derived macrophages through the induction of the L-arginine:NO pathway. This was demonstrated by increased generation of nitrite (NO2-), the stable oxidation product of NO, and by the ability of NG-monomethyl-L-arginine to block both NO generation and parasite killing. A similar NO-dependent effect was observed with interferon gamma-treated cells. Tumor necrosis factor alpha is involved in this process, since both the induction of NO synthase and the killing of parasites caused by anti-**CD23** mAb were inhibited by an anti-tumor necrosis factor alpha mAb. Treatment of noninfected **CD23**+ macrophages with IgE-IC provided protection against subsequent in vitro infection of these cells by Leishmania major promastigotes. Thus, IgE-IC promote killing of L. major by inducing NO synthase in human macrophages.

L20 ANSWER 34 OF 59 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

95318434 EMBASE Document No.: 1995318434. IL-4 induces human B cell maturation and IgE synthesis in SCID-hu mice: Inhibition of ongoing IgE production by in vivo treatment with an IL-4/IL-13 receptor **antagonist**. Carballido J.M.; Schols D.; Namikawa R.; Zurawski S.; Zurawski G.; Roncarolo M.-G.; De Vries J.E.. Department of Human Immunology, DNAX Research Institute, 901 California Avenue,Palo Alto, CA 94304, United States. Journal of Immunology 155/9 (4162-4170) 1995. ISSN: 0022-1767. CODEN: JOIMA3. Pub. Country: United States. Language: English. Summary Language: English.

AB The effect of cytokine treatment on the in vivo maturation and Ig isotype switching of human B cells was studied in a modified SCID-hu mouse model. SCID mice, subcutaneously cotransplanted with small fragments of fetal human thymus and bone (SCID-hu BM/T mice) generated all human leukocyte lineages including T and B lymphocytes, macrophages, and granulocytes. All SCID-hu BM/T mice spontaneously produced human IgM and IgG, whereas IgE and IgA were detected in 37 and 80% of the mice, respectively, indicating

that productive human T-B cell interactions resulting in Ig isotype switching occur in these mice. Administration of IL-4 to SCID-hu BM/T mice enhanced human B cell maturation, as judged by the increase in the percentages of CD45+, CD19+ bone marrow B cells expressing CD20, **CD23**, CD40, sIgM, and sIgD. Furthermore, these cells were also functionally more mature because they spontaneously produced human IgG/IgG4 in vitro and could be induced to secrete human IgE by addition of anti-CD40 mAb alone. In contrast, B cells isolated from PBS- treated mice only produce significant Ig levels after stimulation with anti- CD40 mAb in the presence of exogenous IL-4. IL-4 administration also induced human IgE synthesis in 44% of the mice, which had no serum IgE before treatment. More importantly, ongoing human IgE synthesis in SCID-hu BM/T mice was suppressed by >90% following administration of an IL-4 mutant protein, which acts as an IL-4 and IL-13 receptor **antagonist**. These results suggest that IL-4/IL-13 receptor **antagonists** have potential clinical utility in treating human atopic diseases associated with enhanced IgE production.

L20 ANSWER 35 OF 59 MEDLINE DUPLICATE 5
96274016 Document Number: 96274016. PubMed ID: 8679119. Anti-IgE therapy. Jardieu P. (Department of Immunology, Genentech Inc, San Francisco, CA 94080, USA.) CURRENT OPINION IN IMMUNOLOGY, (1995 Dec) 7 (6) 779-82. Ref: 36. Journal code: 8900118. ISSN: 0952-7915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Controlling the IgE response at either the synthesis level or the effector phase should have a profound impact on the allergic cascade. For more than a decade, researchers have focused on ways of interfering with the binding of IgE to its high-affinity receptor on proinflammatory cells. Several approaches have also been taken to antagonize the complex interplay of cytokines and cell-associated molecules (CD40, **CD23**) that are implicated in IgE synthesis. Recently, anti-IgE **antibodies** have been developed that are potent IgE **antagonists**. These **antibodies** are currently under clinical investigation as potential therapeutics for allergic disease.

L20 ANSWER 36 OF 59 MEDLINE
96084283 Document Number: 96084283. PubMed ID: 8565148. Lovastatin induces differentiation of Mono Mac 6 cells. Weber C; Erl W; Weber P C. (Institut fur Prophylaxe und Epidemiologie der Kreislaufkrankheiten, Ludwig-Maximilians-Universitat, Munchen, Germany.) CELL BIOCHEMISTRY AND FUNCTION, (1995 Dec) 13 (4) 273-7. Journal code: 8305874. ISSN: 0263-6484. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The proliferation of human monocytic Mono Mac 6 cells was significantly retarded by treatment with lovastatin (LOV, 10 microM) for 72 h. Treatment of Mono Mac 6 cells with LOV increased surface protein expression of monocyte-associated CD14 and the integrin-chain CD11b towards levels found in isolated human blood monocytes. These effects were dose-dependent and completely reversed by the isoprenoid precursor mevalonate (MVA). LOV failed to induce growth retardation and upregulation of CD11b or CD14 in the less mature premonocytic U937 cell line. While CD11b expression was comparable in Mono Mac 6 cells treated with LOV (10 microM), TNF (100 U ml-1) or LPS (10 ng ml-1), upregulation of CD14 by LOV was less pronounced. Basal **CD23** expression was unaffected by LOV but markedly reduced by treatment with TNF or LPS. Moreover, LOV enhanced Mono Mac 6 adhesiveness to human umbilical vein endothelial cells to levels found in isolated human blood monocytes, probably due to the increased CD11b and CD14 expression. In conclusion, LOV can induce differentiation of monocytic cells which is reflected by the retardation of growth, expression of CD14 and CD11b, and enhanced adhesiveness.

L20 ANSWER 37 OF 59 MEDLINE
95131073 Document Number: 95131073. PubMed ID: 7829968. Ligation of

CD23 activates soluble guanylate cyclase in human monocytes via an L-arginine-dependent mechanism. Paul-Eugene N; Kolb J P; Sarfati M; Arock M; Ouaaz F; Debre P; Mossalayi D M; Dugas B. (INSERM U 365, Institut Curie, Paris, France.) JOURNAL OF LEUKOCYTE BIOLOGY, (1995 Jan) 57 (1) 160-7. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB Transduction through Fc epsilon R2/**CD23** was analyzed in normal human monocytes using immunoglobulin E (IgE)-anti-IgE immune complexes (IgE ICs) and monoclonal **antibodies** (mAbs) to **CD23**. Anti-**CD23** mAb and IgE IC triggered a time-dependent increase in cGMP and cAMP in interleukin-4-preincubated (**CD23**+) but not in unstimulated (**CD23**-) monocytes. Maximal cGMP and cAMP accumulations were observed 10 and 20 min, respectively, after the onset of **CD23** ligation. The increase in cGMP was inhibited with N omega-monomethyl-L-arginine (L-NMMA), which also partially affected cAMP accumulation. Addition of an anti-**CD23** mAb Fab fragment inhibited the IgE IC- and the anti-**CD23** mAb-induced cGMP and cAMP accumulation, confirming the engagement of **CD23**. In addition, IgE IC and anti-**CD23** mAb induced, at least in some donors, a production of nitrite that was inhibited in the presence of L-NMMA. Taken together, these findings suggest a possible involvement of the nitric oxide synthase pathway in IgE IC-mediated activation of **CD23**+ monocytes.

L20 ANSWER 38 OF 59 MEDLINE

94194138 Document Number: 94194138. PubMed ID: 8144946. Induction of B cell and T cell tolerance in vivo by anti-**CD23** mAb. Morris S C; Lees A; Holmes J M; Jeffries R D; Finkelman F D. (Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD 20814.) JOURNAL OF IMMUNOLOGY, (1994 Apr 15) 152 (8) 3768-76. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB T cell tolerance can be induced by B cell presentation of Ags to naive T cells. To further characterize this mechanism of T cell tolerance induction, we have investigated the effects of injecting mice with an intact rat IgG2a Ab, which binds to the B cell low-affinity Fc epsilon receptor (**CD23**), on the responsiveness of B cells and T cells to rat IgG2a. Our observations indicate that 1) intravenous, subcutaneous, or intraperitoneal injection of this Ab induces antigen-specific B cell and T cell tolerance; 2) both forms of tolerance are induced more completely by injection of rat IgG2a anti-**CD23** mAb than by injection of an equal dose of a control rat IgG2a Ig; and 3) reduced responsiveness to Ag is seen as early as 1 to 3 days after anti-**CD23** mAb injection and reaches maximum levels by 7 days after injection. Although tolerance induced by the injection of soluble proteins has been reported to be characterized by reduced production of IL-2 and IFN-gamma, but normal production of IL-4, injection of mice with rat IgG2a anti-mouse **CD23** mAb greatly decreases the IL-4 response to a rat IgG2a immunogen that normally induces a large IL-4 response.

L20 ANSWER 39 OF 59 MEDLINE DUPLICATE 6

94237998 Document Number: 94237998. PubMed ID: 8182161. Involvement of cyclic AMP and nitric oxide in immunoglobulin E-dependent activation of Fc epsilon RII/**CD23**+ normal human keratinocytes. Becherel P A; Mossalayi M D; Ouaaz F; Le Goff L; Dugas B; Paul-Eugene N; Frances C; Chosidow O; Kilchherr E; Guillosson J J; +. (Molecular Immuno-Hematology Group (CNRS URA 625), Pitie-Salpetriere Hospital, Paris, France.) JOURNAL OF CLINICAL INVESTIGATION, (1994 May) 93 (5) 2275-9. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Epidermal keratinocytes (EK) are exposed to multiple inflammatory stimuli and paracrine factors secreted by various dermal cells (lymphocytes, mast cells, macrophages, fibroblasts) during wounding, cutaneous allergy, and infections. We have previously demonstrated that after stimulation with

interleukin 4 or interferon-gamma, human EK express the low-affinity receptor for IgE (Fc epsilon RII/**CD23**) on their surface. In the present study, we showed that the ligation of **CD23** by IgE/anti-IgE immune complexes or specific monoclonal **antibody** induces a dose-dependent release of interleukin 6 and tumor necrosis factor-alpha from EK. **CD23**-ligation activates the nitric oxide-dependent pathway, as demonstrated by the high levels of nitrites released in cell supernatants, and the accumulation of intracellular cyclic nucleotides in EK. These second messengers are required for IgE-dependent stimulation of cytokine production by these cells, inasmuch as this is completely abolished by the use of cAMP or nitric oxide synthase **antagonists**. Human epithelial keratinocytes may thus participate in IgE-mediated immune responses, through their ability to express functional **CD23** antigen.

L20 ANSWER 40 OF 59 MEDLINE
95048907 Document Number: 95048907. PubMed ID: 7960241.
Lymphoproliferative disease in human peripheral-blood-mononuclear-cell-injected scid mice. II. Role of host and donor factors in tumor generation. Veronesi A; Coppola V; Veronese M L; Menin C; Bruni L; D'Andrea E; Mion M; Amadori A; Chieco-Bianchi L. (Institute of Oncology, Interuniversity Center for Research on Cancer, University of Padua, Italy.) INTERNATIONAL JOURNAL OF CANCER, (1994 Dec 1) 59 (5) 676-83. Journal code: 0042124. ISSN: 0020-7136. Pub. country: United States. Language: English.

AB Intraperitoneal injection of lymphoid cells from EBV+ donors into SCID mice might provide a useful tool for studying the pathways of B-cell lymphomagenesis in man. Since previous studies showed that donor T cells greatly favor B-cell proliferation and tumor generation in this model, we addressed the host and donor factors involved in limiting or promoting lymphoma development. The number of EBV-infected B-cell precursors was crucial, since purified B lymphocytes, which alone were unable to generate tumors, underwent expansion and established tumor masses when the animals were inoculated with an EBV-containing supernatant. Host factors were critical in limiting tumor development; in vivo NK-cell removal allowed purified B cells to expand and proceed to tumors in the absence of T lymphocytes, whereas potentiation of mouse NK-cell activity prevented tumor generation in PBMC- and LCL-injected animals. The T-cell-derived factors that favor lymphomagenesis could not be identified; IL-2, IL-4, IL-6, and soluble **CD23** were not able to promote B-cell expansion, and treatment of PBMC-injected mice with the relevant anti-cytokine anti-sera did not counteract lymphoma development. These experiments also showed that IL-6 plays a minor role, if any, in B-cell lymphoproliferation in this model. Our data indicate that reconstitution of SCID mice with PBMC from EBV+ donors may constitute a useful model for determining the events involved in lymphomagenesis in humans, provided that strict control of all the experimental variables is guaranteed.

L20 ANSWER 41 OF 59 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 7
94324392 EMBASE Document No.: 1994324392. Design of human interleukin-4 **antagonists** inhibiting interleukin-4-dependent and interleukin-13-dependent responses in T-cells and B-cells with high efficiency. Tony H.-P.; Shen B.-J.; Reusch P.; Sebald W.. Theodor-Boveri-Inst. Biowissensch., (Biozentrum), Universitat Wurzburg, Physiologische Chemie II, Am Hubland,D-97074 Wurzburg, Germany. European Journal of Biochemistry 225/2 (659-665) 1994.
ISSN: 0014-2956. CODEN: EJBCAI. Pub. Country: Germany. Language: English. Summary Language: English.

AB Human interleukin-4 possesses two distinct sites for receptor activation. A signalling site, comprising residues near the C-terminus on helix D, determines the efficacy of interleukin-4 signal transduction without affecting the binding to the interleukin-4 receptor .alpha. subunit. A complete **antagonist** and a series of low-efficacy agonist

variants of human interleukin-4 could be generated by introducing combinations of two or three negatively charged aspartic acid residues in this site at positions 121, 124, and 125. One of the double variants, designated [R121D,Y124D]interleukin-4, with replacements of bath Arg121 and Tyr124 by aspartic acid residues was completely inactive in all analysed cellular responses. The loss of efficacy in [R121D,Y124D]interleukin-4 is estimated to be larger than 2000-fold. Variant [R121D,Y124D]interleukin-4 was also a perfect **antagonist** for inhibition of interleukin-13-dependent responses in B-cells and the TF-1 cell line with a K(i) value of approximately 100 pM. In addition, inhibition of both interleukin-4-induced and interleukin-13-induced responses could be obtained by monoclonal **antibody** X2/45 raised against interleukin-4R(ex), the extracellular domain of the interleukin-4 receptor .alpha. subunit. These results indicate that efficient interleukin-4 **antagonists** can be designed on the basis of a sequential two-step activation model. In addition, the experiments indicate the functional participation of the interleukin-4 receptor .alpha. subunit in the interleukin-13 receptor system.

L20 ANSWER 42 OF 59 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 8

1994:539300 Document No.: PREV199497552300. Interleukin-1 receptor **antagonist** protein inhibits the synthesis of IgE and proinflammatory cytokines by allergen-stimulated mononuclear cells. Sim, Tommy C. (1); Hilsmeier, Kimberly A.; Reece, Lisa M.; Grant, J. Andrew; Alam, Rafeul. (1) Div. Allergy Immunol., Dep. Internal Med., CSB-409, 301 University Blvd., Univ. Texas Med. Branch, Galveston, TX 77555-0762 USA. American Journal of Respiratory Cell and Molecular Biology, (1994) Vol. 11, No. 4, pp. 473-479. ISSN: 1044-1549. Language: English.

AB The ability of interleukin-1 (IL-1) to activate diverse cell populations supports its role as a preeminent cytokine in the pathogenesis of chronic inflammation. In this study, we investigated the role of IL-1 and IL-1 receptor **antagonist** protein (IRAP) in the regulation of allergen-induced synthesis of IgE and proinflammatory cytokines. The temporal expression of IL-1-beta and IRAP during 5-day allergen-activated peripheral mononuclear cell (PMNC) cultures suggested differential production of the two cytokines. To determine the influence of IRAP on IL-1-mediated cellular responses, we cultured PMNC from allergic donors with specific allergens in the presence or absence of IRAP pretreatment. Culture supernatants were assayed for IgE and cytokines using specific enzyme-linked immunosorbent assay. IRAP at concentrations 0.01, 0.1, and 1 mu-g/ml decreased the allergen-stimulated IgE synthesis by 33 +- 7%, 05 +- 7%, and 66 +- 5%, respectively (P lt 0.05). Increasing the concentration of allergen did not affect the reduction in IgE synthesis observed in the presence of IRAP. Lipopolysaccharide-stimulated IgE synthesis was also significantly inhibited by IRAP (P lt 0.05). In parallel experiments, anti-IL-1-beta monoclonal **antibody** showed a comparable inhibtory pattern on Ige synthesis (P lt 0.05). IRAP inhibited the synthesis of interleukin-6, tumor necrosis factor-alpha, and granulocyte/macrophage colony-stimulating factor in a dose dependent manner (P lt 0.05); the mean inhibition was 31 +- 4%, 75 +- 5%, and 88 +- 2%, respectively, at 1 mu-g/ml of IRAP. Synthesis of soluble **CD23** was also significantly abrogated by IRAP (P lt 0.05). In addition, there was a significant effect of IRAP on IL-1-beta production in four of six donors. We conclude that IRAP inhibits both allergen- and lipopolysaccharide-induced synthesis of IgE as well as allergen-induced production of proinflammatory cytokines. Taken together, these findings identify novel biologic actions of IRAP as a modulator of the allergic inflammatory response.

L20 ANSWER 43 OF 59 MEDLINE

94173564 Document Number: 94173564. PubMed ID: 7907416. Expression of inflammatory membrane markers by conjunctival cells in chronically treated

patients with glaucoma. Baudouin C; Garcher C; Haouat N; Bron A; Gastaud P. (Department of Ophthalmology, Saint-Roch Hospital, University of Nice, France.) OPHTHALMOLOGY, (1994 Mar) 101 (3) 454-60. Journal code: 7802443. ISSN: 0161-6420. Pub. country: United States. Language: English.

AB PURPOSE: Recent histologic studies of conjunctival tissues in patients who have had long-term treatment for glaucoma have shown in situ an abnormal infiltration by inflammatory cells. In this study, conjunctival inflammatory antigens were investigated in impression cytology specimens from patients who have been and those who have not been treated for glaucoma. METHODS: This study included 107 eyes from 55 patients with primary open-angle glaucoma. Of these, 48 had received prolonged topical treatments, all containing benzalkonium chloride as a preservative. Seven glaucomatous eyes could be examined before any treatment. In addition, the authors examined 11 patients (21 eyes) receiving anticataract eye drops preserved with chlorhexidine and 15 normal untreated subjects (30 eyes). In all patients, immunocytochemistry was performed in impression cytology specimens, using two monoclonal **antibodies** against HLA-DR antigens and receptor to IgE **CD23**. RESULTS: None of the untreated eyes showed reactivity for either monoclonal **antibody**. In contrast, HLA-DR expression by conjunctival cells was found in 43 of 88 treated eyes (mean percentage of reactive cells, 70% +/- 28%) and positive staining for receptor to IgE in 26 of 68 eyes (52% +/- 28% of conjunctival cells). Results were not related to a specific treatment or combination of anti-glaucoma drugs. However, the proportion of positive specimens (3/14 for both antigens) in the group receiving chlorhexidine-containing eye drops was significantly lower than that found in the patients with glaucoma. CONCLUSION: This study showed abnormal expression of inflammatory markers without clinical inflammation at the level of conjunctival cells in repetitive contact with various anti-glaucomatous treatments and their common preservative, benzalkonium chloride. Failure in filtering glaucoma surgery was found to be related to prolonged medical treatment; therefore, a topical sensitization to preservatives and/or anti-glaucoma drugs has been hypothesized. An immunocytologic test thus could be useful for qualitative and quantitative investigation of drug-induced conjunctival inflammation and predict high-risk patients.

L20 ANSWER 44 OF 59 SCISEARCH COPYRIGHT 2003 ISI (R)

94:743708 The Genuine Article (R) Number: PT565. DIFFERENTIAL-EFFECTS OF INTERLEUKIN-2 AND INTERLEUKIN-4 ON IMMUNOMODULATORY ROLE OF PLATELET-ACTIVATING-FACTOR IN HUMAN B-CELLS. PATKE C L; GREEN C G; SHEARER W T (Reprint). TEXAS CHILDRENS HOSP, DEPT ALLERGY IMMUNOL, HOUSTON, TX, 77030 (Reprint); TEXAS CHILDRENS HOSP, DEPT ALLERGY IMMUNOL, HOUSTON, TX, 77030; BAYLOR COLL MED, DEPT PEDIAT, HOUSTON, TX, 77030; BAYLOR COLL MED, DEPT MICROBIOL & IMMUNOL, HOUSTON, TX, 77030. CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY (JUL 1994) Vol. 1, No. 4, pp. 424-432 . ISSN: 1071-412X. Pub. country: USA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Platelet-activating factor (PAF), a naturally occurring phospholipid cytokine, is a potent mediator of allergic and inflammatory reactions, as well as a modulator of immune responses. In the present study we showed that PAF is involved in early B-cell activation, as demonstrated by the increased cyclic AMP (cAMP) generation by PAF in a time- and dose-dependent manner in anti-mu, **antibody**- plus B-cell growth factor-activated normal human peripheral blood B lymphocytes. PAF also regulated differentiation by causing a biphasic response on immunoglobulin M (IgM) production with an inhibitory signal generated at 10(-6) M and a stimulatory signal generated at 10(-8) to 10(-10) M. PAF enhanced IgG and IgA secretion. The regulation exerted by PAF was shown to Be specific because the addition of the PAF **antagonist** CV-3988 abrogated these effects and the inactive form of PAF, lyso PAF, induced neither cAMP generation nor immunoglobulin secretion in normal human B cells. Other cytokines, interleukin-2 (IL-2) and IL-4, potent mediators of the immune response, were unable to elicit a cAMP response in B cells. However, the

addition of PAF (10(-6) M) with either IL-2 or IL-4 enhanced cAMP production above the levels enhanced by the addition of PAF alone. IL-2 or IL-4, individually, stimulated IgM production, yet costimulation with PAF resulted in a differential effect between IL-2 and IL-4. PAF down-regulated the IL-4-induced IgM secretion, whereas the IL-2-induced IgM secretion was enhanced. The presence of CV-3988 returned all values to those obtained with IL-2 or IL-4 alone, demonstrating the specificity of PAF. These data suggest that PAF is an important B-cell immunomodulator which can interact with other leukocyte cell mediators.

L20 ANSWER 45 OF 59 MEDLINE
94163687 Document Number: 94163687. PubMed ID: 8118870. Identification of a T cell membrane protein possibly involved in IL-4-induced B cell immunoglobulin class switching to IgE. Matsushita S; Katz D H. (Division of Immunology, Medical Biology Institute, La Jolla, California 92037.) CELLULAR IMMUNOLOGY, (1994 Feb) 153 (2) 378-91. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB The murine T cell hybridoma line, MBI-1.15, secretes a 17-kDa protein which decreases binding activity of the **CD23** molecule for its natural ligand, IgE. This protein, denoted epsilon receptor-modulating protein (epsilon RMP), was previously characterized and shown to be a novel serine protease. The present studies show that, in addition to modulating **CD23**, epsilon RMP costimulates with IL-4 the de novo synthesis and secretion of IgE and IgG 1 by cultured B cells. Since such costimulating activity is reminiscent of a similar synergism with IL-4 previously observed with cell membranes from activated T cells, we examined isolated membranes from the epsilon RMP-producing MBI-1.15 T cell line for comparable activity; indeed, as shown herein, MBI-1.15 cell membranes do exhibit this synergism. Furthermore, we show that a monoclonal **antibody** (mAb), 2E5B, specific for the 17-kDa soluble form of epsilon RMP, blocks the costimulating activities of both the soluble epsilon RMP and MBI-1.15 T cell membranes for IL-4-induced de novo synthesis of IgE by cultured B cells. This anti-epsilon RMP mAb also detects a 36-kDa membrane-bound protein species which appears to be related to soluble epsilon RMP by immunochemical criteria. The membrane-bound proteins, present on MBI-1.15 T cells, induce germ-line IgE heavy chain transcripts (I epsilon) in I-29 B cells independently of IL-4, and this inductive event is also specifically blocked by the 2E5B anti-epsilon RMP mAb. These findings suggest that T cell membrane-bound epsilon RMP molecules are crucial proteins involved in contact-dependent B cell class switching in the course of IgE biosynthesis. Finally, both IL-4 and epsilon RMP induce I epsilon on I-29 B cells, but neither molecule by itself can induce class switching to IgE synthesis by splenic B cells. This clearly suggests that both epsilon RMP and IL-4 have another important molecular effect (which may or may not be identical) on B cells, that is essential for class switching, but only when both molecules are present simultaneously is the complete mechanism of class switching manifested.

L20 ANSWER 46 OF 59 MEDLINE DUPLICATE 9
95003948 Document Number: 95003948. PubMed ID: 7522713. IgE-dependent activation of Fc epsilon RII/**CD23**+ normal human keratinocytes: the role of cAMP and nitric oxide. Becherel P A; Mossalayi M D; Le Goff L; Ouaaz F; Dugas B; Guillosson J J; Debre P; Arock M. (Molecular Immuno-Hematology Group, CNRS URA 625, Pitie-Salpetriere Hospital, Paris, France.) CELLULAR AND MOLECULAR BIOLOGY, (1994 May) 40 (3) 283-90. Journal code: 9216789. ISSN: 0145-5680. Pub. country: France. Language: English.

AB Epidermal keratinocytes (EK) are exposed to multiple inflammatory stimuli and paracrine factors secreted by various dermal cells (lymphocytes, mast-cells, macrophages, fibroblasts) during wounding, cutaneous allergy and infections. We have previously demonstrated that following stimulation with interleukin-4 (IL-4) or interferon-gamma, human EK

express the low affinity receptor for IgE (Fc epsilon RII/**CD23**) on their surface. In the present study, we showed that the ligation of **CD23** by IgE/anti-IgE immune complexes or specific monoclonal **antibody**, induces a dose-dependent release of interleukin-6 and tumor necrosis factor-alpha from EK. **CD23**-ligation activates the nitric oxide-dependent pathway, as demonstrated by the high levels of nitrites released in cell supernatants, and the accumulation of intracellular cyclic nucleotides in EK. These second messengers are required for IgE-dependent stimulation of cytokine production by these cells, as this is completely abolished by cAMP or NO synthase **antagonists**. Human epithelial keratinocytes may thus participate in IgE-mediated immune responses, through their ability to express functional **CD23** antigen.

L20 ANSWER 47 OF 59 CAPLUS COPYRIGHT 2003 ACS
1993:493523 Document No. 119:93523 Murine and human cytokine (CD40-L) which binds to CD40, and soluble CD40 and CD40 fusion molecules. Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K. (Immunex Corp., USA). PCT Int. Appl. WO 9308207 A1 19930429, 79 pp. DESIGNATED STATES: W: AU, CA, FI, JP, KR, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US8990 19921023. PRIORITY: US 1991-783707 19911025; US 1991-805723 19911205.

AB The title CD40-L mols. are disclosed, as are related DNA sequences, vectors, and transformed host cells. The murine and human CD40-L polypeptides bind to the extracellular binding region of a CD40 receptor. Also provided are a CD40/IgG1 Fc region fusion protein and a sol. CD40 protein (sCD40) comprising the extracellular portion of CD40; both the CD40/Fc and sCD40 can inhibit CD40-L or anti-CD40 monoclonal **antibody**-induced B-cell stimulation, interleukin-4-induced IgE stimulation, and interleukin-4-induced **CD23** induction in B-cells. Construction is described of a CD40/Fc DNA for prodn. of a fusion protein for use in detecting cDNA clones encoding a CD40 ligand. Also described are selection of a cell line putatively expressing CD40-L, prepn. of a cDNA library for expression cloning of murine CD40-L, cross-species hybridization methodol. used to isolate a human CD40-L homolog, anti-allergy therapeutic effects of sCD40 and CD40/Fc fusion protein, etc. Interaction of CD40 with its ligand was evidently the principal mol. interaction responsible for T-cell contact-dependent induction of B-cell growth and differentiation to both antigen-specific **antibody** prodn. and polyclonal Ig secretion.

L20 ANSWER 48 OF 59 MEDLINE DUPLICATE 10
94065191 Document Number: 94065191. PubMed ID: 7902377. Effects of IL-13 on phenotype, cytokine production, and cytotoxic function of human monocytes. Comparison with IL-4 and modulation by IFN-gamma or IL-10. de Waal Malefyt R; Figdor C G; Huijbens R; Mohan-Peterson S; Bennett B; Culpepper J; Dang W; Zurawski G; de Vries J E. (Department of Human Immunology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104.) JOURNAL OF IMMUNOLOGY, (1993 Dec 1) 151 (11) 6370-81. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Recently, we described the cloning and expression of a human cDNA which is the homologue to P600, a gene transcribed by mouse Th2 clones. Based on its activities on human monocytes and B cells this gene was designated IL-13. In the present study we investigated the effects of IL-13 alone or in combination with IL-4, IFN-gamma, or IL-10 on human monocytes. IL-13 induced significant changes in the phenotype of monocytes. Like IL-4, it enhanced the expression of CD11b, CD11c, CD18, CD29, CD49e (VLA-5), class II MHC, CD13, and **CD23**, whereas it decreased the expression of CD64, CD32, CD16, and CD14 in a dose-dependent manner. IL-13 induced up-regulation of class II MHC Ag and its down-regulatory effects on CD64, CD32, and CD16 expression were prevented by IL-10. IFN-gamma could also partially prevent the IL-13-induced down-regulation of CD64, but not that

of CD32 and CD16. However, IL-13 strongly inhibited spontaneous and IL-10- or IFN-gamma-induced ADCC activity of human monocytes toward anti-D coated Rh+ erythrocytes, indicating that the cytotoxic activity of monocytes was inhibited. Furthermore, IL-13 inhibited production of IL-1 alpha, IL-1 beta, IL-6, IL-8, IL-10, IL-12 p35, IL-12 p40, macrophage inflammatory protein-1 alpha, granulocyte/macrophage-CSF, granulocyte-CSF, IFN-alpha, and TNF alpha by monocytes activated with LPS. In contrast, IL-13 enhanced the production of IL-1 ra by these cells. Similar results on cytokine production were observed or have been obtained with IL-4. Thus IL-13 shares most of its activities on human monocytes with IL-4, but no additive or synergistic effects of IL-4 and IL-13 on human monocytes were observed, suggesting that these cytokines may share common receptor components. Taken together, these results indicate that IL-13 has anti-inflammatory and important immunoregulatory activities.

L20 ANSWER 49 OF 59 MEDLINE

94242922 Document Number: 94242922. PubMed ID: 8186375. Inhibitors of protein tyrosine kinases and protein tyrosine phosphatases suppress IL-4-induced **CD23** expression and release by human B lymphocytes. Kolb J P; Abadie A. (U365 INSERM, Interferons et Cytokines, Institut Curie, Paris, France.) EUROPEAN CYTOKINE NETWORK, (1993 Nov-Dec) 4 (6) 429-38. Journal code: 9100879. ISSN: 1148-5493. Pub. country: France. Language: English.

AB The pleiotropic lymphokine IL-4 is a growth and differentiation factor for human B cells. IL-4 induces the expression of the **CD23** (Fc epsilon RII) molecule on B lymphocytes and promotes the release of its soluble form (sCD23); the cleavage fragments of the latter have been reported to modulate IL-4-dependent IgE biosynthesis. In the present work, we have tested the effects of inhibitors of protein tyrosine kinases (PTK) and protein phosphatases (PP) on the induction by IL-4 of the membrane and soluble forms of **CD23**. The PTK inhibitors genistein and lavendustin A were found to suppress, in a dose-dependent way, the induction by IL-4 of **CD23** membrane expression as well as **CD23** release by resting and SAC-preactivated B lymphocytes. No such suppression was detected with inhibitors of serine and threonine kinases. The addition of the protein tyrosine phosphatase (PTP) inhibitor sodium orthovanadate also resulted in a marked decrease in **CD23** induction by IL-4. Cell viability was little affected by these inhibitors. However, a diminution of the large activated B cell population was observed, which correlated with an inhibition of the entry in the S phase. Partial inhibition of sCD23 release was also observed with okadaic acid and calyculin A, two inhibitors of serine/threonine PP, but only at concentrations which block PP1 in addition to PP2A. These results suggest that protein tyrosine phosphorylation and dephosphorylation may play a major role in IL-4 signalling. This conclusion was strengthened by the observation that a mAb anti-CD45, a membrane tyrosine phosphatase, inhibited IL-4-induced sCD23 release by B lymphocytes.

L20 ANSWER 50 OF 59 SCISEARCH COPYRIGHT 2003 ISI (R)

93:40829 The Genuine Article (R) Number: KG694. FUNCTIONAL INTERACTION BETWEEN BETA-2-ADRENOCEPTOR AGONISTS AND INTERLEUKIN-4 IN THE REGULATION OF **CD23** EXPRESSION AND RELEASE AND IGE PRODUCTION IN HUMAN. PAULEUGENE N (Reprint); KOLB J P; CALENDA A; GORDON J; KIKUTANI H; KISHIMOTO T; MENCIAHUERTA J M; BRAQUET P; DUGAS B. INST CURIE, INSERM, U196, 26 RUE ULM, F-75231 PARIS 05, FRANCE (Reprint); UNIV PARIS 11, CRNS, URA 1354, F-91405 ORSAY, FRANCE; INST HENRI BEAUFOUR, IMMUNOALLERGOL LAB, F-91952 LES ULIS, FRANCE; UNIV BIRMINGHAM, DEPT IMMUNOL, BIRMINGHAM B15 2TT, W MIDLANDS, ENGLAND; OSAKA UNIV, DEPT IMMUNOL, OSAKA, JAPAN. MOLECULAR IMMUNOLOGY (FEB 1993) Vol. 30, No. 2, pp. 157-164. ISSN: 0161-5890. Pub. country: FRANCE; ENGLAND; JAPAN. Language: ENGLISH. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Normal human peripheral blood mononuclear cells (PBMC) produced IgE

when stimulated with IL-4. In the present report it was shown that beta2-adrenoceptor agonists, salbutamol and fenoterol, potentiated the IL-4-induced IgE production without significantly affecting the expression of the low affinity receptor for IgE at the cell surface of monocytes and B lymphocytes. However, beta2-adrenoceptor agonists were shown to enhance at day 7 the IL-4-induced release of the soluble form of **CD23** (sCD23) by PBMC. This effect was specific since a beta-adrenoceptor **antagonist**, D,L-propranolol, inhibited the IL-4-induced IgE production by these cells. Alternatively, the beta2-adrenoceptor agonists inhibited the production by these cells of interferon-gamma (IFN-gamma) but did not affect the production of IL-4 when stimulated with phytohemagglutinin A + a phorbol ester. These data suggest that beta2-adrenoceptor agonists influence the IL-4-induced IgE production in humans by enhancing the release of sCD23 and inhibiting the production of endogenous IFN-gamma. In addition to the effect on the IL-4-induced IgE production it was shown that beta2-adrenoceptor agonists potentiated the effect of IL-4 on a human promonocytic cell line, U 937, by enhancing **CD23** expression and release and by inducing the differentiation of these cells into monocyte-like cells. Taken together, these data indicate that beta2-adrenoceptor agonists potentiated the effect of IL-4 and that this functional interaction is different considering the cell-lineage and the stage of differentiation of these cells.

L20 ANSWER 51 OF 59 MEDLINE

93172604 Document Number: 93172604. PubMed ID: 8382323. Suppression of IgE production by IPD-1151T (suplatast tosilate), a new dimethylsulfonium agent: (2). Regulation of human IgE response. Yanagihara Y; Kiniwa M; Ikizawa K; Shida T; Matsuura N; Koda A. (Clinical Research Center for Allergy, National Sagamihara Hospital, Kanagawa, Japan.) JAPANESE JOURNAL OF PHARMACOLOGY, (1993 Jan) 61 (1) 31-9. Journal code: 2983305R. ISSN: 0021-5198. Pub. country: Japan. Language: English.

AB The ability of IPD-1151T to suppress the induction of human IgE synthesis was investigated with an in vitro model of IgE production mediated by an allergen-specific helper T cell line (SN-4) from a patient allergic to Japanese cedar pollen. IPD-1151T induced a concentration-dependent suppression of purified allergen (Cry j 1)-dependent IgE synthesis in autologous B cell cultures mediated by SN-4, without significantly affecting the IgG synthesis. In addition, the production of interleukin 4 (IL-4) by Cry j 1-activated SN-4 as well as that by phytohemagglutinin (PHA)-stimulated peripheral blood mononuclear cells (PBMC) of normal donors was inhibited in a concentration-dependent manner by the agent. Interestingly, IPD-1151T clearly depressed PHA-induced expression of IL-4 mRNA in normal PBMC, indicating that this agent inhibits IL-4 gene transcription. However, IPD-1151T had no antagonistic action on IL-4, since neither IL-4-induced expression of low-affinity IgE receptor (Fc epsilon RII/**CD23**) on normal B cells nor soluble Fc epsilon RII release from IL-4-stimulated B cells was affected by the agent. On the other hand, IPD-1151T had no effect on the production of interferon-gamma by both Cry j 1-stimulated SN-4 and anti-CD3 monoclonal **antibody** -activated T cells of normal donors. These results suggest that the selective suppression of IgE synthesis by IPD-1151T results from the inhibition of IL-4 production by T cells at the gene level.

L20 ANSWER 52 OF 59 MEDLINE

93172603 Document Number: 93172603. PubMed ID: 8382322. Suppression of IgE production by IPD-1151T (suplatast tosilate), a new dimethylsulfonium agent: (1). Regulation of murine IgE response. Yanagihara Y; Kiniwa M; Ikizawa K; Yamaya H; Shida T; Matsuura N; Koda A. (Clinical Research Center for Allergy, National Sagamihara Hospital, Kanagawa, Japan.) JAPANESE JOURNAL OF PHARMACOLOGY, (1993 Jan) 61 (1) 23-30. Journal code: 2983305R. ISSN: 0021-5198. Pub. country: Japan. Language: English.

AB The effect of IPD-1151T, a new dimethylsulfonium compound, on the IgE response was investigated in the mouse system. The oral administration of

IPD-1151T to immunized BALB/c mice suppressed the primary IgE **antibody** response and depressed the elevation of serum IgE levels, whereas the same treatment did not affect the IgG **antibody** response. The enhanced expression of low-affinity IgE receptor (Fc epsilon RII/**CD23**) on the spleen cells of immunized mice was also inhibited by IPD-1151T administration. It was further demonstrated from the adoptive transfer experiment that IPD-1151T, administered to hapten-primed B cell donors, but not to carrier-primed T cell donors, exerted its suppressive influence on the hapten-specific secondary IgE **antibody** response in irradiated syngeneic recipients. Interestingly, IPD-1151T concentration-dependently inhibited the production of interleukin 4 (IL-4) by D10G4.1, known to be a typical Th2 clone. However, IPD-1151T did not suppress the production of IgE and IgG1 by normal splenic B cells stimulated with lipopolysaccharide and IL-4. Moreover, IL-4-induced expression of Fc epsilon RII on normal spleen cells was not inhibited by the agent. These results strongly suggest that the IgE-suppressive activity of IPD-1151T is most likely due to the inhibition of IL-4 production at the T cell level.

L20 ANSWER 53 OF 59 MEDLINE

93208310 Document Number: 93208310. PubMed ID: 1296802. Expression of **CD23** by human bone marrow stromal cells. Fourcade C; Arock M; Ktorza S; Ouaaz F; Merle-Beral H; Mentz F; Kilchherr E; Debre P; Mossalayi M D. (Laboratoire d'Immunologie, CHU Pitie-Salpetriere, Paris, France.) EUROPEAN CYTOKINE NETWORK, (1992 Nov-Dec) 3 (6) 539-43. Journal code: 9100879. ISSN: 1148-5493. Pub. country: France. Language: English.

AB **CD23** is a surface antigen expressed by a variety of human hematopoietic cells and shown to display multiple biological functions. In present work, we assayed **CD23** expression by human bone marrow (BM) or by stromal cells derived from this tissue. While freshly isolated BM-cells showed low **CD23** expression, a subset of long term BM-culture (LTBMC)-derived stromal cells expressed **CD23** mRNA at high levels in their steady state and secreted soluble **CD23** in their culture supernatants. To assay the role of **CD23** in LTBMC, these cultures were initiated in the presence of neutralizing anti-**CD23** mAb. A dramatic decrease in total numbers of hematopoietic cells and CFU-GM recovery was observed in these cultures as compared to controls. These data suggest a role of **CD23** expression in stroma cell functions and further confirm the ability of this antigen to regulate human hematopoietic cell development.

L20 ANSWER 54 OF 59 MEDLINE DUPLICATE 11

92040269 Document Number: 92040269. PubMed ID: 1834581. Pharmacological modulation of the antigen-induced expression of the low-affinity IgE receptor (Fc epsilon RII/**CD23**) on rat alveolar macrophages. Mencia-Huerta J M; Dugas B; Boichot E; Petit-Frere C; Paul-Eugene N; Lagente V; Capron M; Liu F T; Braquet P. (Departement d'Immunologie, Institut Henri Beaufour, Les Ulis, France.) INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1991) 94 (1-4) 295-8. Journal code: 0404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.

AB Brown-Norway (BN) rats were sensitized by 3 aerosol exposures to ovalbumin (OA; 10 mg/ml) at days 1, 3 and 14. At day 21, the rats were challenged with the antigen or vehicle by aerosol. Alveolar macrophages (AM) were obtained by bronchoalveolar lavage and the expression of Fc epsilon RII/**CD23** was assessed by flow cytometry after staining with the BB10 monoclonal **antibody**. A maximum of 74% of the AM from sensitized and challenged BN rats expressed FC epsilon RII/**CD23** 24 h after OA exposure, compared to 12% of the cells from rats exposed to vehicle. Sprague-Dawley rats were passively sensitized by intravenous injection of 0.1 or 0.05 ml/kg mouse ascitic fluid containing dinitrophenyl (DNP)-specific monoclonal IgE (2682-1) and after 24 h exposed to an aerosol of 5 mg/ml of DNP-bovine serum albumin for 30 min. In this case also, antigen exposure induced the expression of Fc epsilon RII/

CD23 on 75% AM, compared to 17% AM from saline-challenged rats. Such an induction of Fc epsilon RII/**CD23** on AM was, however, not observed when the animals were challenged with either histamine, serotonin or acetylcholine by aerosol. The antigen-induced expression of Fc epsilon RII/**CD23** on AM was inhibited upon treatment of the rats with ketotifen or beclomethasone. In addition, oral or aerosol administration of respectively BN 50730 or BN 52021 (two structurally unrelated platelet-activating factor **antagonists**), inhibited the antigen-induced Fc epsilon RII/**CD23** expression on AM, indicating the participation of this lipid mediator in this process.

L20 ANSWER 55 OF 59 MEDLINE

91223680 Document Number: 91223680. PubMed ID: 1673878. Fc epsilon receptor II/**CD23**-positive lymphocytes in atopic dermatitis. I. The proportion of Fc epsilon RII+ lymphocytes correlates with the extent of skin lesion. Takigawa M; Tamamori T; Horiguchi D; Sakamoto T; Yamada M; Yoshioka A; Toda K; Imamura S; Yodoi J. (Department of Dermatology, Hamamatsu University School of Medicine, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 May) 84 (2) 275-82. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Cells expressing Fc receptors for IgE (Fc epsilon RII) were identified in the peripheral blood from patients with atopic dermatitis and with eczematous dermatitis, and normal non-atopic subjects by using monoclonal **antibodies** to human lymphocyte Fc epsilon RII, and to lymphoid cell-surface antigens by immunofluorescence staining. Based on the extent of the dermatitis patients were classified as severe (greater than 50% skin surface involved), moderate (50-10%) and mild (less than 10%). Patients with severe and moderate atopic dermatitis had 5.9% and 5.7% Fc epsilon RII+ peripheral blood mononuclear cells (PBMC), respectively, that were significantly higher than percentages in mild atopic dermatitis patients (2.6%), severe to moderate eczematous dermatitis patients (2.3%), mild eczematous dermatitis patients (2.2%) and normal individuals (1.7%)(0.05 greater than P). In severe and moderate atopic dermatitis patients, 10% of Fc epsilon RII+ PBMC were T cells that preferentially expressed CD8, and the remainder B cells and monocytes. Fc epsilon RII+ T cells comprised 1% of peripheral T cells, while half or more of peripheral B cells expressed Fc epsilon RII. In mild atopic dermatitis patients, eczematous dermatitis patients and normal subjects. Fc epsilon RII were expressed exclusively on 25-35% of peripheral B cells. Short-term treatment and long-term follow-up of atopic dermatitis patients revealed that changes in the skin condition were related closely to fluctuations in the proportion of Fc epsilon RII+ PBMC. Total serum IgE levels and atopic respiratory allergy did not influence the percentage of Fc epsilon RII+ PBMC. These findings suggest that the percentage of Fc epsilon RII+ PBMC reflects the extent of atopic dermatitis.

L20 ANSWER 56 OF 59 MEDLINE

91223044 Document Number: 91223044. PubMed ID: 1709049. Independent regulation of interleukin 4 (IL-4)-induced expression of human B cell surface **CD23** and IgM: functional evidence for two IL-4 receptors. Rigley K P; Thurstan S M; Callard R E. (Department of Immunology, Institute of Child Health, London, UK.) INTERNATIONAL IMMUNOLOGY, (1991 Feb) 3 (2) 197-203. Journal code: 8916182. ISSN: 0953-8178. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Activation of human B cells with interleukin 4 (IL-4) is known to result in increased expression of **CD23** (the low-affinity receptor for IgE) and sIgM. However, whereas **CD23** expression is increased by several B cell mitogens, including phorbol 12-myristate 13-acetate, Epstein-Barr virus, anti-immunoglobulin (Ig), and IL-4, surface IgM (sIgM) expression is increased only with IL-4, suggesting that expression of each surface antigen is regulated independently. This was confirmed in three different ways. First, in dose-response experiments, it was shown that 10 times the concentration of IL-4 was required for **CD23** than for

sIgM expression. Similar or even higher concentrations of IL-4 were required for proliferation. In fact, optimal sIgM expression was obtained in some experiments with concentrations of IL-4 (1-5 units/ml) which had little or no effect on either **CD23** expression or B cell proliferation. Secondly, IL-4 is known to activate the phosphatidyl inositol pathway in human B cells followed 8-10 min later by an increase in cAMP. Pharmacologically mimicking this pathway by brief exposure of resting B cells to phorbol dibutyrate plus ionomycin followed 10 min later with dibutyryl cAMP resulted in an increase in expression of **CD23** but not sIgM. Thirdly, CD19 monoclonal **antibody**, which inhibits B cell proliferation in response to IL-4 plus anti-Ig, was found to inhibit IL-4-induced **CD23** but not sIgM expression. These results show that **CD23** and sIgM expression are regulated independently and are consistent with the existence of two separate signal transduction pathways stimulated by IL-4, which may be coupled to distinct IL-4 receptors.

L20 ANSWER 57 OF 59 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
91353239 EMBASE Document No.: 1991353239. Itch and atopic dermatitis: Clinical and experimental studies. Wahlgren C.-F.. Department of Dermatology, Karolinska Hospital, Karolinska Institute,Stockholm, Sweden. Acta Dermato-Venereologica, Supplement -/165 (4-53) 1991.
ISSN: 0365-8341. CODEN: AVSUAR. Pub. Country: Norway. Language: English. Summary Language: English.

AB The aims of the study were to develop and evaluate methods for quantitative measurement of itch, to investigate the perception of itch in patients with atopic dermatitis (AD), and to measure itch in such patients during treatment with H1-receptor **antagonists** or cyclosporin A, thereby exploring possible mechanisms in the pathogenesis of itch in AD. In a double-blind, randomized, placebo-controlled, cross-over study of 30 AD patients using a potent, topical, antipruritic corticosteroid, two methods for measuring itch both successfully detected the itch-relieving effect of the corticosteroid. The two methods comprised new portable data-loggers (Pain-Track) for continuous recording of itch, and conventional visual analogue scale (VAS) forms for retrospective recording. The main advantages of the Pain-Track method are possibilities for frequent sampling, surveillance of compliance, and analysis of a large amount of data. Induction and measurement of experimental histamine-induced itch were studied in 38 healthy subjects. It was shown that pruritic stimuli should be presented in a random order so as to avoid systematic errors in the perception of itch. Two rating scales, a seven-stepped non-verbal scale on a Pain-Track logger, and a 100-mm VAS on a potentiometer, were found valid for continuous recording of itch. The perception of experimental itch was studied in 32 AD patients and 32 healthy controls. The itch responses provoked by wool fibres were significantly stronger in AD patients than in controls, whereas the histamine-induced dose-response curves for itch did not differ significantly between the two groups, who discriminated equally well between weak and strong histamine stimuli. No increased skin mast cell releasability was shown in vivo to compound 48/80 in AD patients. Their itch responses to the different pruritic stimuli did not correlate with clinical itch intensity, eczema score or serum IgE-level. In a double-blind, randomized, placebo-controlled, cross-over study of 25 AD patients, the effect on clinical itch of a sedative (clemastine) and of a non-sedative (terfenadine) antihistamine did not differ from that of placebo, although both drugs had a pronounced H1-receptor-antagonizing effect in the skin and clemastine was significantly sedative. These findings support the view that histamine is not the major pruritogen in AD, and that sedation is not necessarily associated with itch relief. In a double-blind, randomized, placebo-controlled, cross-over study of 10 AD patients, 10 days' treatment with cyclosporin A (CSA), 5 mg/kg/day, significantly reduced itch intensity, eczema score and the number of peripheral blood eosinophils. Relapses were seen within 2-30 days of

completion of CSA therapy. In at least 50% of the patients, CSA reduced the number of CD3+, CD4+, HLA-DR+, IgE+, **CD23**+ (low-affinity Fc-IgE receptor+), intercellular adhesion molecule-1+, and EG2+ (activated eosinophils) cells in lesional skin. The changes of itch magnitude in the patients did not strictly parallel any specific change in the occurrence of these cell surface markers. The mechanism of action for the antipruritic effect of CSA remains unclear, but it is hypothesized that cytokines may be involved in the pathogenesis of itch in AD.

L20 ANSWER 58 OF 59 MEDLINE
91346548 Document Number: 91346548. PubMed ID: 2102812. Regulatory effects of IL-4 on human B-cell response to IL-2. Galanaud P; Karray S; Llorente L. (INSERM Unite 131.32, Clamart, France.) EUROPEAN CYTOKINE NETWORK, (1990 May-Jun) 1 (2) 57-64. Ref: 48. Journal code: 9100879. ISSN: 1148-5493. Pub. country: France. Language: English.
AB Interleukin-4 (IL-4) counteracts a number of the direct effects of interleukin-2 (IL-2) on B-cells. We here summarize and extend our results, obtained in two different experimental systems, on the antagonism between these two major interleukins. IL-4 inhibits the effect of IL-2 on the proliferation as well as the differentiation of B-type chronic lymphocytic leukemia (B-CLL) cells. When B-CLL cells are activated by anti-mu Ab in the presence of IL-4, this latter enhances the expression of the p55 as well as the p70/75 chain of the IL-2 receptor. In contrast IL-4 profoundly suppresses the number of high affinity binding sites for IL-2 on in vitro activated B-CLL cells. Such a discrepancy between the suppression of IL-2 binding sites and the enhancement of each component of the heterodimeric IL-2 receptor, is as far as we know, yet undescribed. The interaction of IL-4 with its own receptors might influence the state of p55-p70/75 complex association or act on a third subunit of the IL-2 receptor. When used alone, IL-4 enhances the expression of other activation molecules by B-CLL cells: **CD23**, DR antigen. Similarly IL-4 can concomitantly enhance the specific response of normal B-cells while suppressing the action of IL-2. When normal human B-cells are specifically stimulated by an insolubilized antigen, IL-4 alone induces an expansion of the number of specific antigen-binding cells. In contrast IL-4 profoundly suppresses the generation of antigen-induced IL-2-dependent specific IgM **antibody** forming cells.(ABSTRACT TRUNCATED AT 250 WORDS)

L20 ANSWER 59 OF 59 MEDLINE
89358095 Document Number: 89358095. PubMed ID: 2527805. Soluble fragments of the low-affinity IgE receptor (**CD23**) inhibit the spontaneous migration of U937 monocytic cells: neutralization of MIF-activity by a **CD23 antibody**. Flores-Romo L; Cairns J A; Millsum M J; Gordon J. (Department of Immunology, University of Birmingham, U.K.) IMMUNOLOGY, (1989 Aug) 67 (4) 547-9. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.
AB U937 monocytic cells were found to respond by diminished spontaneous migration when confronted with affinity-purified soluble fragments of the low-affinity receptor for IgE (FcER2/**CD23**). Unlike B lymphoma cells, U937 cells could not be activated to respond with enhanced DNA synthesis through their membrane-bound **CD23** antigen by MHM6, a monoclonal **antibody** within the **CD23** cluster. MHM6 did, however, effectively neutralize the U937-directed MIF (migration inhibition factor) activity contained within the soluble **CD23** preparations. The findings not only suggest a role for soluble **CD23** as a novel cytokine at sites of inflammation but also indicate different functions for the membrane-bound forms expressed on B cells and monocytes.

=> s l2 and "clone C11"
L21 0 L2 AND "CLONE C11"

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=> d his

     (FILE 'HOME' ENTERED AT 10:30:16 ON 23 APR 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:30:38 ON
     23 APR 2003
L1      2419928 S ANTIBODY
L2         3300 S L1 AND CD23
L3           90 S L2 AND CHIMERIC
L4            9 S L3 AND HUMANIZED
L5            9 DUP REMOVE L4 (0 DUPLICATES REMOVED)
L6            0 S L3 AND BINDING AFFINITY
L7            6 S L2 AND BINDING AFFINITY
L8            6 DUP REMOVE L7 (0 DUPLICATES REMOVED)
L9          218 S ANTIBODY BINDING AFFINITY
L10           0 S L9 AND ANTI-CD23
L11           0 S L9 AND CD23
L12           0 S L9 AND FC EPSILON RECEPTOR II
L13           0 S L9 AND "RSSKSLLYKDGKTYLN"
L14           0 S L9 AND "1X109 KA PER M"
L15           0 S L2 AND BIOCORE ASSAYS
L16           0 S L2 AND BIACORE ASSAY
L17         111 DUP REMOVE L9 (107 DUPLICATES REMOVED)
L18           0 S L17 AND CD23 ANTIBODY
L19          88 S L2 AND ANTAGONIST
L20          59 DUP REMOVE L19 (29 DUPLICATES REMOVED)
L21           0 S L2 AND "CLONE C11"

=> dup remove l3
PROCESSING COMPLETED FOR L3
L22          38 DUP REMOVE L3 (52 DUPLICATES REMOVED)

=> d l22 1-38 cbib abs

L22  ANSWER 1 OF 38  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
     1
2003:138690  Document No.: PREV200300138690. Temperature effect on IgE binding
     to CD23 versus FcepsilonRI. Chen, Bing-Hung; Kilmon, Michelle
     A.; Ma, Check; Caven, Timothy H.; Chan-Li, Yee; Shelburne, Anne E.;
     Tombes, Robert M.; Roush, Eric; Conrad, Daniel H. (1). (1) Department of
     Microbiology and Immunology, Virginia Commonwealth University, Box 980678,
     MCV Station, Richmond, VA, 23298-0678, USA: dconrad@hsc.vcu.edu USA.
     Journal of Immunology, (February 15 2003) Vol. 170, No. 4, pp. 1839-1845.
     print. ISSN: 0022-1767. Language: English.
AB   A chimeric soluble CD23, consisting of the
     extracellular domain of mouse CD23 and a modified leucine zipper
     (lz-CD23), has been shown to inhibit IgE binding to the
     FcepsilonRI. A similar human CD23 construct was also shown to
     inhibit binding of human IgE to human FcepsilonRI. In both systems, the
     inhibition was found to be temperature dependent; a 10-fold molar excess
     of lz-CD23 gave 90-98% inhibition at 4degreeC, dropping to
     20-30% inhibition at 37degreeC. Surface plasmon resonance analysis of lz-
     CD23 binding to an IgE-coated sensor chip suggested that the
     effective concentration of lz-CD23 was lower at the higher
     temperatures. Analysis of 125I-IgE binding to CD23+-Chinese
     hamster ovary cells also indicated that increased temperature resulted in
     a lower percentage of IgE capable of interacting with CD23. In
     contrast, IgE interacts more effectively with FcepsilonRI+-rat basophilic
     leukemia cells at 37degreeC compared with 4degreeC. The results support
     the concept that the open and closed IgE structures found by
     crystallography interact differently with the two IgE receptors and
     suggest that temperature influences the relative percentage of IgE in the
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respective structural forms. Changes in **CD23** oligomerization also plays a role in the decreased binding seen at physiological temperatures.

L22 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2003 ACS
2002:594705 Document No. 137:139366 Immunoregulatory **antibodies** and uses thereof. Hariharan, Kandasamy; Hanna, Nabil (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002060485 A2 20020808, 103 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2621 20020131. PRIORITY: US 2001-772938 20010131; US 2001-855717 20010516; US 2001-985646 20011105; US 2001-PV331187 20011109.

AB A combination **antibody** therapy for treating B cell malignancies using an immunoregulatory **antibody**, esp. an anti-B7, anti-**CD23**, or anti-CD40L **antibody**, and a B-cell depleting **antibody**, esp. anti-CD19, anti-CD20, anti-CD22 or anti-CD37 **antibody**, is provided. Preferably, the combination therapy will comprise anti-B7 and anti-CD20 **antibody** administration. IDEC-131, IDEC-114, and Rituxan monoclonal **antibodies** are of special interest.

L22 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2003 ACS
2002:594704 Document No. 137:153822 **CD23** antagonistic **antibodies** for treatment of neoplastic disorders. Hariharan, Kandasamy; Hanna, Nabil; Braslawsky, Gary R.; Pathan, Nuzhat (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002060484 A1 20020808, 88 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2620 20020131. PRIORITY: US 2001-772938 20010131; US 2001-855717 20010516; US 2001-985646 20011105.

AB Methods and kits for the treatment of neoplastic disorders comprising the use of a **CD23** antagonist are provided. These **CD23** antagonists are monoclonal, polyclonal, **chimeric**, humanized or primatized **antibodies**, e.g. IDEC-152. The **CD23** antagonist may be used alone or in combination with radiotherapeutic or chemotherapeutic agents. In particularly preferred embodiments the **CD23** antagonists may be used to treat B cell chronic lymphocytic leukemia (B-CLL).

L22 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L22 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2003 ACS
2002:51297 Document No. 136:117380 Treatment of B cell malignancies using combination of B cell depleting **antibody** and immune modulating **antibody** related applications. Hanna, Nabil; Hariharan, Kandasamy (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002004021 A1 20020117, 88 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US15677 20010516. PRIORITY: US 2000-PV217706 20000712; US 2001-772938 20010131.
AB A combination **antibody** therapy for treating B cell malignancies using an immunoregulatory **antibody**, esp. an anti-B7, anti-**CD23**, or anti-CD40L **antibody** and a B cell depleting **antibody**, esp. anti-CD19, anti-CD20, anti-CD22 or anti-CD37 **antibody** is provided. Preferably, the combination therapy will comprise anti-B7 and anti-CD20 **antibody** administration.

L22 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2003 ACS
2002:833304 Document No. 137:309495 Use of **CD23** antagonists for the treatment of neoplastic disorders. Hariharan, Kandasamy; Hanna, Nabil; Braslawsky, Gary; Pathan, Nuzhat (USA). U.S. Pat. Appl. Publ. US 2002159996 A1 20021031, 42 pp., Cont.-in-part of U.S. Ser. No. 772,938. (English). CODEN: USXXCO. APPLICATION: US 2001-985646 20011105. PRIORITY: US 2001-772938 20010131.
AB Methods and kits for the treatment of neoplastic disorders comprising the use of a **CD23** antagonist are provided. The **CD23** antagonist may be used alone or in combination with chemotherapeutic agents. In particularly preferred embodiments the **CD23** antagonists may be used to treat B cell chronic lymphocytic leukemia (B-CLL). The **CD23** antagonists are anti-**CD23** **antibodies**, particularly IDEC 152. IDEC 152 synergizes with chemotherapeutic agents in inducing apoptosis of cancer cells.

L22 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2003 ACS
2002:773675 Document No. 137:293559 Human Fc.epsilon.RII receptor homolog. Wood, William I.; Goddard, Audrey; Gurney, Austin; Yuan, Jean; Baker, Kevin P.; Chen, Jian (Genentech, Inc., USA). Eur. Pat. Appl. EP 1247817 A2 20021009, 37 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL. (English). CODEN: EPXXDW. APPLICATION: EP 2002-12909 19990308. PRIORITY: US 1998-PV84637 19980507; EP 1999-912321 19990308.
AB The authors disclose the cloning and recombinant expression of a protein (PRO792) which exhibits extracellular domain homol. to human **CD23**
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L22 ANSWER 8 OF 38 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2002370873 EMBASE B cell positive selection by soluble self-antigen. Julien S.; Soulas P.; Garaud J.-C.; Martin T.; Pasquali J.-L.. Dr. J.-L. Pasquali, Laboratoire d'Immunopathologie, Institut d'Hematologie/d'Immunologie, 1 place de l'hopital, 67091 Strasbourg Cedex, France. Jean-Louis.Pasquali@hemato-ulp.u-strasbg.fr. Journal of Immunology

169/8 (4198-4204) 15 Oct 2002.
Refs: 49.
ISSN: 0022-1767. CODEN: JOIMA3. Pub. Country: United States. Language: English. Summary Language: English.

AB It is well established that autoreactive B cells undergo negative selection. This stands in paradox with the high frequency of so-called natural autoreactive B cells producing low affinity polyreactive autoantibodies with recurrent specificities, suggesting that these B cells are selected on the basis of their autoreactivity. We previously described two transgenic mouse lines (with and without IgD) producing a human natural autoantibody (nAAb) that binds ssDNA and human Fc.gamma.. In the absence of human IgG, nAAb-transgenic B cells develop normally. By crossing these mice with animals expressing knockin **chimeric** IgG with the human Fc.gamma., we now show that the constitutive expression of **chimeric** IgG promotes the increase of nAAb-expressing B cells. This positive selection is critically dependent on the presence of IgD, occurs in the spleen, and concerns all mature B cell subsets, with a relative preferential enrichment of marginal zone B cells. These data support the view that soluble self-Ags can result in positive clonal selection.

L22 ANSWER 9 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:370946 Document No.: PREV200200370946. **Antibodies** against the stalk region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239. http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.

AB The stalk region of human **CD23** comprising a.a. 48-153 was expressed in E. coli and purified. In addition a **chimeric** human **CD23** was prepared consisting of the extracellular region of **CD23** linked to a modified leucine zipper (LZ-**CD23**). Polyclonal antisera were produced in rabbits and shown to block binding of IgE to **CD23** both on cell surfaces as well as the interaction of LZ-**CD23** with IgE in an ELISA based assay. The antisera was also shown to inhibit IgE synthesis in an anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose dependent and essentially complete blockage of IgE production was seen at a relatively low dose of anti-stalk. FACS analysis using **CD23**+B lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal **antibodies** against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

L22 ANSWER 10 OF 38 MEDLINE DUPLICATE 2
2002224456 Document Number: 21957817. PubMed ID: 11962725. Anti-**CD23** monoclonal **antibody** inhibits germline Cepsilon transcription in B cells. Yabuuchi Shingo; Nakamura Takehiko; Kloetzer William S; Reff Mitchell E. (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A **chimeric** macaque/human (PRIMATIZED) anti-**CD23** **antibody**, p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 **antibody**-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect

on **CD23** mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface **CD23**, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L22 ANSWER 11 OF 38 MEDLINE
2002663816 Document Number: 22311125. PubMed ID: 12423314. Necessity of the stalk region for immunoglobulin E interaction with **CD23**.
Chen Bing-Hung; Ma Check; Caven Timothy H; Chan-Li Yee; Beavil Andrew; Beavil Rebecca; Gould Hannah; Conrad Daniel H. (Department of Microbiology and Immunology, Virginia Commonwealth University, Richmond, VA 23298, USA.) IMMUNOLOGY, (2002 Nov) 107 (3) 373-81. Journal code: 0374672. ISSN: 0019-2805. Pub. country: England: United Kingdom. Language: English.
AB Previously, a soluble mouse **CD23** chimera, composed of an N-terminal trimeric isoleucine zipper motif (lz) followed by the entire extracellular region (amino acids 48-331) of **CD23** (lz-CD2348-331), was prepared and exhibited strong binding to rodent immunoglobulin E (IgE). In the current study, we report the construction of a similar human **chimeric** protein (lz-huCD2345-321), as well as a series of murine **chimeric** lz-**CD23** mutants with incremental portions of stalk deleted, to further investigate the role of the stalk region in mediating the **CD23**-IgE interaction. All **chimeric** proteins were designed such that the predicted heptad structure of the stalk was retained. IgE binding, as determined by the capacity to inhibit 125I-IgE from binding to FcepsilonRI-bearing RBL-2H3 cells, and by surface plasmon-resonance analysis using an IgE-coated sensor chip, was unchanged from the original lz chimera and the binding parameters were similar to those of cell-surface **CD23**. The minimal murine chimera that retained IgE-binding activity was lz-CD23139-331, which still contains 35 amino acids of the stalk region. When the lz motif was linked to **CD23** amino acid 157 (or higher), significant IgE-binding capacity was lost. With human lz-**CD23**, as with mouse, deletion of the stalk greatly reduced IgE-binding ability. In summary, the data support the concept that at least a portion of the stalk region of **CD23** plays a crucial role in maintaining high-affinity/avidity interaction with IgE. The lz-**CD23** constructs represent a possible alternative for both blocking the IgE/FcepsilonRI interaction and inhibiting IgE production by B lymphocytes.

L22 ANSWER 12 OF 38 MEDLINE DUPLICATE 3
2001485563 Document Number: 21418923. PubMed ID: 11527816. Anti-CD20 monoclonal **antibody** treatment of human herpesvirus 8-associated, body cavity-based lymphoma with an unusual phenotype in a human immunodeficiency virus-negative patient. Perez C L; Rudoy S. (Departamento Virologia, Instituto Nacional de Enfermedades Infecciosas-ANLIS Dr. Carlos G. Malbran, Av. Velez Sasrsfield 563 (1281), Buenos Aires, Argentina.. Cperez@anlis.gov.ar) . CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2001 Sep) 8 (5) 993-6. Journal code: 9421292. ISSN: 1071-412X. Pub. country: United States. Language: English.
AB Human herpesvirus 8 (HHV-8), or Kaposi's sarcoma-associated herpesvirus, is a gammaherpesvirus first detected in Kaposi's sarcoma tumor cells and subsequently in primary effusion lymphoma (PEL) tumor cells and peripheral blood mononuclear cells from PEL patients. PEL has been recognized as an individual nosologic entity based on its distinctive features and consistent association with HHV-8 infection. PEL is an unusual form of body cavity-based B-cell lymphoma (BCBL). It occurs predominantly in human immunodeficiency virus (HIV)-positive patients but occasionally also in elderly HIV-negative patients. We describe a case of PEL, with ascites, bilateral pleural effusions, and a small axillary

lymphadenopathy, in a 72-year-old HIV-negative man. PCR performed on a lymph node specimen and in liquid effusion was positive for HHV-8 and negative for Epstein-Barr virus. The immunophenotype of the neoplastic cells was B CD19+ CD20+ CD22+ with coexpression of CD10 and **CD23** and with clonal kappa light chain rearrangement. The patient was treated with Rituximab, a **chimeric** (human-mouse) anti-CD20 monoclonal **antibody**. Thirteen months later, the patient continued in clinical remission. This is the first report of an HHV-8-associated BCBL in an HIV-negative patient in Argentina.

L22 ANSWER 13 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:186685 Document No.: PREV200200186685. Induction of apoptosis by IDEC-152 (anti-**CD23**) in lymphoma cells. Pathan, Nuzhat (1); Hariharan, Kandasamy (1); Hopkins, Michael; Saven, Alan; Reff, Mitchell (1); Hanna, Nabil (1); Grint, Paul (1). (1) IDEC Pharmaceuticals, San Diego, CA USA. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 367a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB IDEC-152 is a primatized monoclonal **antibody** to human **CD23**, the low-affinity receptor for IgE on B cells that has been implicated in the regulation of IgE synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses IgE synthesis. IDEC-152 is currently in clinical trials for use in allergic asthma. **CD23** is also expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a **chimeric** monoclonal **antibody** to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain **CD23** positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of apprx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong **antibody** dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of **CD23**, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L22 ANSWER 14 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2001:291320 Document No.: PREV200100291320. Novel respiratory tract B cell populations contribute to antiviral immunity. Baumgarth, Nicole (1); Herzenberg, Leonore A.. (1) University of California, One Shields Ave, Davis, CA, 95616 USA. FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A365. print. Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001 ISSN: 0892-6638. Language: English. Summary Language: English.

AB We present data demonstrating that a constant number of B cells with the phenotype: IgMhi IgDlo B220lo CD11b+ **CD23**- CD43+ CD5+ are present in the respiratory tract of wildtype mice during life. These lung parenchyma B cells, which make up roughly 5% of the B cell population in adult lungs, are able to reconstitute the pool of peritoneal cavity B-1

cells when adoptively transferred into lethally irradiated recipients; thus, demonstrating that they belong to the B-1 cell population. In B-1/B-2 allotype **chimeric** mice established by neonatal anti-IgM **antibody** treatment and transfer of congenic allotype mismatched peritoneal cavity B cells, we furthermore demonstrate that a second population of B-1 cells is present in the lung. Importantly 10-color FACS analysis revealed that this population of B-1 cells lacks expression of CD5, one of the hallmarks of B-1 cells, and lacks expression of IgM and IgD. Instead these B cells express surface IgA. Approximately 30% of the total IgA+ lung B cell population is B-1 cell-derived. B-1 cell-derived IgA is present in the bronchoalveolar lavage, and some of this IgA recognizes influenza A virus prior to any infection. In contrast, only B-2 cells produce influenza virus specific IgA induced by infection. Hence, local respiratory tract IgA is similar to systemic IgM in that it is derived from two distinct B cell populations, one (B-1) that provides natural Ig and one (B-2) that provides the antigen-specific Ig response.

L22 ANSWER 15 OF 38 MEDLINE DUPLICATE 4
2001672134 Document Number: 21574715. PubMed ID: 11718214.
Lymphoplasmacytic lymphoma/immunocytoma: towards a disease-targeted treatment?. Clavio M; Quintino S; Venturino C; Ballerini F; Varaldo R; Gatto S; Galbusera V; Garrone A; Grasso R; Canepa L; Miglino M; Pierri I; Gobbi M. (Dept. of Internal Medicine, University of Genoa, Genova, Italy.) JOURNAL OF EXPERIMENTAL AND CLINICAL CANCER RESEARCH, (2001 Sep) 20 (3) 351-8. Ref: 46. Journal code: 8308647. ISSN: 0392-9078. Pub. country: Italy. Language: English.

AB Lymphoplasmacytic-lymphoplasmacytoid lymphoma (LPL)/Waldenstrom's macroglobulinemia (WM) or immunocytoma (IMC) consists of diffuse proliferation of small mature B lymphocytes, plasmacytoid lymphocytes, and plasma-cells. The nosographic definition includes the lack of histological, immunophenotypic, cytogenetic, and molecular markers considered specific of other types of lymphoma. The cells show surface Ig (usually IgM), B-cell-associated antigens and display the CD5-, **CD23**- and CD10- phenotype, which allows for differential diagnosis from B-CLL and mantle cell lymphoma. t(9;14)(p13;q32) chromosomal translocation has been found in 50% of all LPL cases. The cytogenetic rearrangement juxtaposes the PAX-5 gene, which encodes for an essential transcription factor for B-cell proliferation and differention, to the Ig heavy chain gene. The combination of chlorambucil and prednisone holds as the standard treatment and seems to guarantee good control of the disease in most patients. Similar therapeutic results have been described with the combination of cyclophosphamide, vincristine, prednisone with (CHOP) or without doxorubicin (CVP), or with a combination of other alkylating agents and prednisone. Nucleoside analogues, alone or in combination with alkylating agents and anthracyclines, provide good salvage therapy for IMC and being increasingly employed as first line therapy. In a multicentric European trial Foran et al. administered the **chimeric** anti-CD20-monoclonal **antibody** (Rituximab) to 28 patients with previously treated IMC. Seven out of 25 evaluable patients (28%) achieved a partial response. Byrd et al. examined the outcome of 7 previously treated WM patients who received weekly infusions of rituximab (375 mg/m2). Therapy was well tolerated by all patients, and there was no decrease in cellular immune function, or significant infectious morbidity. Partial responses were noted in three of these patients, including two with fludarabine-refractory disease. These data suggest that rituximab exerts clinical activity on heavily pre-treated patients with WM. Furthermore, Weide et al. first reported that WM-associated polyneuropathy can be treated effectively with a combination of chemotherapy and the anti-CD20 monoclonal **antibody** rituximab. Most published trials exploring the efficacy of high dose treatment as salvage therapy for relapsed or refractory low grade non Hodgkin's lymphoma have included prevalently follicular or lymphocytic lymphomas. In selected high risk patients radioimmunotherapy with autologous stem-cell rescue, and

myeloablative therapy followed either by autologous stem cell transplantation (SCT) or allogeneic SCT might represent an alternative strategy.

L22 ANSWER 16 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2001:175390 Document No.: PREV200100175390. Anti-**CD23** monoclonal **antibody** (IgE inhibition involves the Fc portion of the molecules. Yabuuchi, Shingo (1); Nakamura, Takehiko (1); Kloetzer, William S.; Reff, Mitchell E.. (1) Seikagaku Corporation Central Research Laboratories, Tokyo Japan. Journal of Allergy and Clinical Immunology, (February, 2001) Vol. 107, No. 2, pp. S181. print. Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology New Orleans, Louisiana, USA March 16-21, 2001 ISSN: 0091-6749. Language: English. Summary Language: English.

L22 ANSWER 17 OF 38 MEDLINE DUPLICATE 5
2001219184 Document Number: 21205870. PubMed ID: 11309819. Monoclonal **antibody** FMC7 detects a conformational epitope on the CD20 molecule: evidence from phenotyping after rituxan therapy and transfectant cell analyses. Serke S; Schwaner I; Yordanova M; Szczepek A; Huhn D. (Department of Hematology and Oncology, Humboldt University, Berlin, Germany.. serke@charite.de) . CYTOMETRY, (2001 Apr 15) 46 (2) 98-104. Journal code: 8102328. ISSN: 0196-4763. Pub. country: United States. Language: English.
AB Numerous studies have reported that monoclonal **antibody** (mAb) FMC7 detects an antigen present on only a subset of circulating B lymphocytes. In particular, this mAb may distinguish typical B-cell chronic lymphocytic leukemia (FMC7 negative) from other types of B-cell non-Hodgkin lymphoma (B-NHL; FMC7 positive). We treated patients with B-NHL with Rituxan, a **chimeric** CD20 mAb, and observed abrogation of staining not only with prototype CD20 mAb B-1 but also with mAb FMC7. To investigate the relation between antigens CD20 and FMC7, we performed mutual blocking studies that showed mutual inhibition of FMC7 and CD20. In addition, FMC7 modulated **CD23** expression and confirmed the presence of mAb B-1 in B-lymphoblastoid cell lines CESS and JVM. Transient transfection of myeloid cell line K562 with plasmid containing CD20-encoding cDNA produced de novo expressions of CD20 and FMC7. Our data indicate that FMC7 binds to a particular conformation of the CD20 antigen, probably to a multimeric CD20 complex. We assume that FMC7 stains positively only when CD20 antigen is present in high densities and in the postulated multimeric complex formation.

L22 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2003 ACS
2000:861519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Deboer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2000072879 A1 20001207, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.
AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors (UgE Fc receptor type I and **CD23**), expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and **chimeric** mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L22 ANSWER 19 OF 38 MEDLINE DUPLICATE 6

2000384038 Document Number: 20304490. PubMed ID: 10845922. Engagement of CD11b and CD11c beta2 integrin by **antibodies** or soluble **CD23** induces IL-1beta production on primary human monocytes through mitogen-activated protein kinase-dependent pathways. Rezzonico R; Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine, University Hospital, Geneva, Switzerland.. rezzonic@unice.it) . BLOOD, (2000 Jun 15) 95 (12) 3868-77. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB beta2 integrins are involved in the recruitment of leukocytes to inflammatory sites and in cellular activation. We demonstrate that ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2 integrins by mAbs or soluble **chimeric CD23** (sCD23) on human freshly isolated monocytes rapidly stimulates high levels of interleukin-1beta production. This induction takes place at the transcriptional level and is regulated by members of the mitogen-activated protein kinase (MAPK) family. Indeed, stimulation of monocytes through engagement of CD11b or CD11c results in the phosphorylation and activation of ERK1, ERK2, and p38/SAPK2 MAP kinases. U0126, a potent inhibitor of the upstream activator of ERK1/2, ie, MEK1/2, suppresses IL-1beta messenger RNA (mRNA) expression in a dose-dependent fashion, showing the implication of this pathway in the transcriptional control of IL-1beta production. On the other hand, inhibition of p38 by SB203580 indicates that this MAPK is involved in the control of IL-1beta production at both transcriptional and translational levels. Together these data demonstrate that ligation of CD11b and CD11c beta2 integrins by mAbs or sCD23 fusion proteins triggers the activation of 2 distinct MAPK signaling pathways that cooperate in controlling IL-1beta synthesis at different levels. (Blood. 2000;95:3868-3877)

L22 ANSWER 20 OF 38 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

2001:311682 Document No.: PREV200100311682. Monoclonal **antibody** FMC7 detects a conformational epitope on the CD20 molecule: Evidence from phenotyping after Rituxan therapy and transfectant cell analyses. Serke, Stefan (1); Schwaner, Ingo (1); Yordanova, Maya (1); Szczepek, Agnes; Huhn, Dieter (1). (1) Department Hematology and Oncology, Humboldt-University, Berlin Germany. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 160a. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology. ISSN: 0006-4971. Language: English. Summary Language: English.

AB Numerous studies have reported that monoclonal **antibody** (MoAb) FMC7 detects an antigen present on only a subset of B lymphocytes. The use of FMC7 has been suggested for discrimination of typical B-CLL (FMC7 negative) from the varieties of other leukemic phase B-NHL (FMC7 positive). During treatment of B-NHL patients with Rituxan, a **chimeric** anti-CD20 MoAb, we have observed not only abrogation of staining with prototype anti-CD20 MoAb B-1, but also of staining with MoAb FMC7. To further investigate the relationship between CD20 and FMC7 antigens we have performed mutual blocking studies. Those studies revealed a mutual inhibition of FMC7 and CD20 MoAbs. When tested on B cell lines CESS and JVM, MoAb FMC7 induced a modulation of **CD23**-expression to the extent as known, and confirmed herein, for MoAb B-1. Finally, upon transient transfection of myeloid cell-line K562 with CD20-encoding mammalian expression vector, de novo expression of both CD20 and FMC7 antigen was observed. Our data indicate that MoAb FMC7 binds to a particular conformation of CD20 antigen, probably to a multimeric CD20 complex. Our data implicate that MoAb FMC7 yields positive staining only when CD20 antigen is present at high density and in the postulated particular multimeric complex formation.

L22 ANSWER 21 OF 38 MEDLINE DUPLICATE 7

2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE

inhibition in B cells by anti-**CD23** monoclonal **antibodies** is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **CD23**, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal **antibodies** to human **CD23** were generated from cynomolgus macaques immunized with purified soluble **CD23** (sCD23). Four of the five primate **antibodies** blocked the binding of IgE complexes to **CD23** positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate **antibodies** were utilized to construct **chimeric** macaque/human (PRIMATIZED((R))) monoclonal **antibodies**. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate **antibody**, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal **antibody** MHM6 recognizes human **CD23** at a different epitope than primate **antibody** 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of **CD23** to an IgG receptor. These data also imply that neither bivalent cross-linking of **CD23** alone or inhibition of **CD23** binding to its natural ligands is sufficient to inhibit IgE production.

L22 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2003 ACS

1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L22 ANSWER 23 OF 38 SCISEARCH COPYRIGHT 2003 ISI (R)

1998:947017 The Genuine Article (R) Number: 146NG. Production of a **chimeric** form of **CD23** that is oligomeric and blocks IgE binding to the Fc epsilon RI. Kelly A E; Chen B H; Woodward E C; Conrad D H (Reprint). VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, BOX 980678, MCV STN, RICHMOND, VA 23298 (Reprint); VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, RICHMOND, VA 23298. JOURNAL OF IMMUNOLOGY (15

DEC 1998) Vol. 161, No. 12, pp. 6696-6704. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The low affinity receptor for IgE (Fc epsilon RII/**CD23**) has previously been shown to interact with IgE with a dual affinity. Three **chimeric** constructs were created containing the lectin domain (amino acids 172-188) or the ''neck'' and lectin domain (amino acids 157-188) attached to subunits of oligomeric proteins. All chimeras were incapable of interacting with IgE with either a high or low affinity, indicating that the alpha-helical stalk of **CD23** is important for orienting the lectin heads such that an interaction with IgE can occur. This concept received further support in that a **chimeric** **CD23** composed of the human **CD23** stalk and the mouse **CD23** lectin head bound mouse IgE with a dual affinity, but could only bind rat IgE with a low affinity. Effort was next concentrated on a construct consisting of the entire extracellular (EC) region of **CD23**, A mutation to the first cleavage site of **CD23** (C1M) resulted in a more stable molecule as determined by a decrease of soluble **CD23** release, A soluble **chimeric** EC-C1M was prepared by attaching an isoleucine zipper to the amino terminus (IzEC-C1M), The interaction with IgE by IzEC-C1M was found to be superior to that seen with EC-**CD23**. The IzEC-C1M could inhibit binding of IgE to both **CD23** and the high affinity receptor for IgE, Fc epsilon RI, providing further evidence for a strong interaction with IgE, Fc epsilon RT inhibition (similar to 70%) was seen at equimolar concentrations of IzEC-C1M, implying the effectiveness of this chimera and suggesting its potential therapeutic value.

L22 ANSWER 24 OF 38 MEDLINE DUPLICATE 8

97188350 Document Number: 97188350. PubMed ID: 9036935. The high-affinity receptor for IgE is the predominant IgE-binding structure in lesional skin of atopic dermatitis patients. Klubal R; Osterhoff B; Wang B; Kinet J P; Maurer D; Stingl G. (Department of Dermatology, University of Vienna Medical School, Austria.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1997 Mar) 108 (3) 336-42. Journal code: 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB While the skin of most patients with atopic dermatitis (AD) is known to contain IgE-bearing cells, the contribution of the various IgE-binding structures to this phenomenon is not fully understood. To address this issue, we eluted cell-bound IgE from cryostat sections of lesional AD skin by acid treatment and performed reconstitution experiments with IgE in the absence or presence of reagents directed against the currently known IgE-binding structures. We found that incubation of acid-treated sections, with either **chimeric** or serum IgE, resulted in the appearance of sizable numbers of anti-IgE-reactive cells. This cellular IgE loading could be entirely prevented by preincubation of the sections with the anti-Fc epsilonRI alpha MoAb 15-1 but not with either **antibodies** against Fc epsilonRII/**CD23** and Fc gammaRII/CD32 or with alpha-lactose. To exclude the possibility that acid treatment of tissue sections may have adversely influenced the IgE-binding capacity of IgE receptors other than Fc epsilonRI, we performed an identical series of experiments on AD skin samples that, as an exception, were essentially devoid of anti-IgE-reactive cells. Again, no IgE loading was detected when these sections were preincubated with anti-Fc epsilonRI alpha MoAbs. In contrast, preincubation of the sections with alpha-lactose and/or MoAbs against Fc epsilonRII/**CD23** or Fc gammaRII/CD32 did not affect IgE loading. Together with the observations that anti-Fc epsilonRI alpha-reactive and IgE-binding cells are largely overlapping populations and include cells of the Langerhans cell/dendritic cell lineage, mast cells, and a few dermal dendrocytes and eosinophils, our results demonstrate that Fc epsilonRI is the predominant and, perhaps, the only biologically relevant IgE-binding structure on histogenetically

and functionally diverse cell populations of AD skin.

L22 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L22 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L22 ANSWER 27 OF 38 MEDLINE DUPLICATE 9
96298736 Document Number: 96298736. PubMed ID: 8671640. Phenotype of B cells responding to the thymus-independent type-2 antigen polyvinyl pyrrolidinone. Whitmore A C; Haughton G; Arnold L W. (Department of Microbiology and Immunology, School of Medicine, University of North Carolina, Chapel Hill 27599, USA.) INTERNATIONAL IMMUNOLOGY, (1996 Apr) 8 (4) 533-42. Journal code: 8916182. ISSN: 0953-8178. Pub. country: ENGLAND: United Kingdom. Language: English.
AB We have determined the origin and cell surface phenotype of B cells producing **antibody** in response to immunization with the non-self TI-2 antigen polyvinyl pyrrolidinone (PVP). We report that the responding cells are derived from precursors in adult bone marrow and display the phenotype characteristic of B-1 cells. By use of allotype marked **chimeric** mice, constructed by reconstituting lethally irradiated

recipients with adult bone marrow and peritoneal B-1 lymphocytes of recognizably different Ig allotypes, immunized with 1 microgram PVP, we found that although a substantial part of the total IgM produced in these chimeras bore the allotype of the transferred peritoneal B-1 cells, essentially all of the anti-PVP IgM expressed the allotype of the adult bone marrow. Fifteen of 16 hybridomas derived from a normal PVP-immune adult mouse bore N nucleotides at the V-D and D-J junctions of their heavy chain CDR3 regions, indicating their origin from precursors in the adult bone marrow. By use of ELISA spot analysis, we found the cells responding to PVP to be localized in the spleens of normal immunized mice. We then used multiparameter flow cytometric sorting to determine the cell surface phenotype of these cells. We found that the cells producing anti-PVP were greatly enriched in a small subpopulation with the phenotypic characteristics of B-1 cells; they were B220intermediate, CD5low, IgMhigh, IgDlow, CD43+ and **CD23**-. This subpopulation was also enriched for all cells producing IgM, regardless of specificity (the so-called 'spontaneous' **antibody**). We conclude that the B-1 phenotype is more likely a marker for a state of differentiation than for a discrete lineage of B cells.

L22 ANSWER 28 OF 38 MEDLINE
95248110 Document Number: 95248110. PubMed ID: 7730644. Characterization of a complement receptor 2 (CR2, CD21) ligand binding site for C3. An initial model of ligand interaction with two linked short consensus repeat modules. Molina H; Perkins S J; Guthridge J; Gorka J; Kinoshita T; Holers V M. (Howard Hughes Medical Institute, Washington University School of Medicine, St. Louis, MO 63110, USA.) JOURNAL OF IMMUNOLOGY, (1995 May 15) 154 (10) 5426-35. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Human CR2 (CD21, EBV receptor) is an approximately 145-kDa receptor and a member of the regulators of complement activation gene family. Regulators of complement activation proteins are characterized by the presence of repeating motifs of 60 to 70 amino acids that are designated short consensus repeats (SCR). CR2 serves as a receptor for four distinct ligands. Three of these ligands (complement C3, gp350/220 of EBV, and **CD23**) interact with the amino terminal 2 of 16 SCR (SCR 1 and 2). Previous studies have determined that at least four sites are important in allowing CR2 to efficiently bind EBV. Two of these sites are also important for binding mAb OKB7, a reagent that blocks both EBV and iC3b/C3dg binding to CR2. We have identified and characterized important sites of iC3b ligand binding by utilizing human-mouse CR2 chimeras, a rat anti-mouse CR2 mAb designated 4E3 that blocks receptor binding to C3, and human CR2-derived peptides. In addition to demonstrating an important role for the same sequence in SCR 1 that is part of the mAb OKB7 and EBV binding site, we have identified a new region within SCR 2 that interacts with C3. These results, when compared with a model of a dual SCR solution structure derived from human factor H SCR, predict that two distinct largely surface-exposed sites on CR2 interact with iC3b. A relative twist of 130 degrees about the long axis of the second SCR in this model would be necessary for these sites to form a single patch for iC3b binding on CR2.

L22 ANSWER 29 OF 38 SCISEARCH COPYRIGHT 2003 ISI (R)
95:285519 The Genuine Article (R) Number: QU825. ANALYSIS OF MURINE SOLUBLE FC-EPSILON-RII SITES OF CLEAVAGE AND REQUIREMENTS FOR DUAL-AFFINITY INTERACTION WITH IGE. BARTLETT W C; KELLY A E (Reprint); JOHNSON C M; CONRAD D H. VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, BOX 980678, MCV STN, RICHMOND, VA, 23298 (Reprint); VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, RICHMOND, VA, 23298. JOURNAL OF IMMUNOLOGY (01 MAY 1995) Vol. 154, No. 9, pp. 4240-4246. ISSN: 0022-1767. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The low-affinity receptor for IgE (FC epsilon RII/**CD23**) is a

type II integral membrane protein with an extracellular C-terminal sequence homologous to C-type animal lectins. Between this region and the membrane is a repetitive sequence predicted to form an alpha-helical coiled-coil and is termed the stalk region. The FC epsilon RII is proteolytically cleaved when at the cell surface in this stalk region. Both the 38 K-d and 28 K-d major released fragments were isolated from culture media and N-terminal sequencing demonstrated that the cleavage sites were in the third and fourth repeat domains, respectively. The identified sites show no apparent similarity with the cleavage sites previously identified in human FC epsilon RII Recent studies have demonstrated that the intact FC epsilon RII interacts with IgE with a dual-affinity, resulting from a multivalent interaction with the IgE Fc region; mutant FC epsilon RII that have a disruption of the alpha-helical coiled-coil have a single low-affinity interaction consistent with a monomeric interaction with IgE. The soluble FC epsilon RII were shown to interact with IgE with an affinity similar to these mutant FC epsilon RII. Preparation of a **chimeric** FC epsilon RII in which the transmembrane and cytoplasmic regions were replaced with sequences from Ly-49 revealed that these regions played no role in the multimeric association of the FC epsilon RII necessary for dual-affinity interaction with IgE. In addition, a full-sized soluble FC epsilon RII construct was expressed, and this molecule demonstrated increased capacity to interact with IgE.

L22 ANSWER 30 OF 38 MEDLINE DUPLICATE 10

96148598 Document Number: 96148598. PubMed ID: 8550069. Regulation and targeting of T-cell immune responses by IgE and IgG **antibodies**.
Bheekha Escura R; Wasserbauer E; Hammerschmid F; Pearce A; Kidd P; Mudde G C. (Department of Immuno-Dermatology, SANDOZ Research Institute, Vienna, Austria.) IMMUNOLOGY, (1995 Nov) 86 (3) 343-50. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A set of **chimeric antibodies** with identical F(ab')2 fragments specific for the hapten 5-iodo-4-hydroxyl-3-nitrophenacetyl (NIP), but with different human Fc parts (gamma 1, gamma 2, gamma 3, gamma 4, epsilon), was used to compare the role of IgG and IgE **antibodies** in antigen presentation by human Epstein-Barr virus (EBV) B cells. Two or three molecules of NIP were coupled to one molecule of Der pI (Der pI-(3)NIP), a major allergen of Dermatophagoides pteronyssinus. Both monomeric IgG and performed complexes of various Der pI/IgG ratios failed to bind significantly to the Fc receptor for IgG on B cells (Fc gamma RII; CD32). Binding of IgG3 (> IgG1)-containing complexes (optimal ratio of antigen to **antibody** = 1:1) could be enhanced by increasing the number of haptens per Der pI molecule to nine or more. However, antigen presentation mediated by IgG and CD32 was not seen with either pulsed B cells or B cells that were allowed to capture the IgG complexes during the whole stimulation period. IgE binding to **CD23** and subsequent IgE-mediated antigen presentation was seen under all conditions tested. Even monomeric immune complexes (IC) (Der pI-(3)NIP/IgE), in the absence of **CD23** cross-linking, induced an immune response. As the number of natural epitopes for human **antibodies** on Der pI was less than five, we conclude that, in vivo, complexes consisting of Der pI/IgG will be directed to antigen-presenting cells expressing the high-affinity receptor for IgG (CD64), whereas IgE will allow antigen presentation by **CD23** -expressing cells, including B cells.

L22 ANSWER 31 OF 38 MEDLINE

95317800 Document Number: 95317800. PubMed ID: 7797246. Functional significance of **CD23**- on **CD23**-transfected Th2 clone.
Nambu M; Hagen M; Sandor M; Sacco R E; Kwack K; Lynch R G. (Department of Pathology, College of Medicine, University of Iowa, Iowa City 52242, USA.) IMMUNOLOGY LETTERS, (1995 Jan) 44 (2-3) 163-7. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB **CD23**, a low-affinity IgE Fc receptor, is not displayed on most resting T cells but its expression has been shown to be transiently induced in vivo and in vitro on some CD4+ T cells [1-4] and in vivo on CD8+ T cells by IgE-secreting hybridoma tumors [5]. To investigate the functional role of **CD23** on T cells, we inserted a **CD23** construct into an expression vector driven by a CD2 promoter and transfected it into a murine Th2 clone D10.G4.1 (D10). We stimulated the transfected D10 cells (D10.3M.24) with anti-TCR **antibody** in the presence or absence of IgE, and measured IL-4, IL-5 and IL-6 production in the culture supernatants. Activation of D10.3M.24 cells by anti-TCR **antibody** induced greater levels of IL-4, IL-5 and IL-6 production, when the TCR and **CD23** were co-crosslinked by TNP anti-TCR and IgE anti-TNP **antibodies**. IgG anti-TNP **antibody** did not enhance lymphokine production by D10.3M.24 cells. The enhanced lymphokine production by IgE was blocked by monoclonal anti-**CD23** **antibody**. IgE anti-TNP **antibody** did not enhance lymphokine production by the wild-type D10 cells induced by TNP anti-TCR **antibody**. These studies show that when co-crosslinked with the TCR, **CD23** can modulate the lymphokine production in activated Th2 cells. Since **CD23** binds to IgE and also binds to CD21 [6], a complement receptor commonly expressed on B cells, T-cell **CD23** could play an immunoregulatory role during cognate T-B cell interaction and during IgE **antibody** responses.

L22 ANSWER 32 OF 38 MEDLINE DUPLICATE 11
93388325 Document Number: 93388325. PubMed ID: 8397173. Antigen focusing by specific monomeric immunoglobulin E bound to **CD23** on Epstein-Barr virus-transformed B cells. Santamaria L F; Bheekha R; van Reijsen F C; Perez Soler M T; Suter M; Bruijnzeel-Koomen C A; Mudde G C. (Swiss Institute of Allergy and Asthma Research, Davos.) HUMAN IMMUNOLOGY, (1993 May) 37 (1) 23-30. Journal code: 8010936. ISSN: 0198-8859. Pub. country: United States. Language: English.

AB Monomeric IgE bound to the low-affinity receptor for IgE (FcERII-**CD23**) on EBV-transformed human B cells selectively enhances binding of antigen and therefore presentation to specific T-cell clones. To demonstrate the role of monomeric IgE in antigen focusing, we have made use of a system consisting of human T-cell clones specific for Der-P1 (major allergen of the Dermathophagoides pteronyssinus), Der-P1 coupled to NIP (Der-P1-NIP), and the commercially available **chimeric** (human-murine) monoclonal IgE **antibodies** with specificity for the hapten NIP. We have found that monomeric IgE binds to **CD23** and remains detectable on the surface of the B cells for a period of at least 16 hours at 37 degrees C. Pulsing of these IgE-anti-NIP (1 microgram/ml) treated B cells for 1 hour at 37 degrees C with low amounts (10 ng/ml) of Der-P1-NIP antigen allows the B cells to stimulate Der-P1-specific T cells. Even with IgE concentrations as low as 20 ng/ml, which were not detectable by immunofluorescence, we were able to induce a significant T-cell response. Furthermore, ongoing specific T-cell-B-cell interactions were not inhibited by the presence of high concentrations of nonspecific IgE molecules (incubated with up to 25 micrograms/ml) on the surface of the B cells. Our data confirm the hypothesis that IgE, bound by either **CD23** or the high-affinity receptor for IgE, potentiates the immune response. Therefore, IgE may be seen as the fourth general mechanism for antigen capture by (nonspecific) antigen-presenting cells.

L22 ANSWER 33 OF 38 MEDLINE DUPLICATE 12
92112647 Document Number: 92112647. PubMed ID: 1530929. Immunoglobulin E-binding site in Fc epsilon receptor (Fc epsilon RII/**CD23**) identified by homolog-scanning mutagenesis. Bettler B; Texido G; Raggini S; Ruegg D; Hofstetter H. (Department of Biotechnology, Ciba-Geigy Ltd., Basel, Switzerland.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Jan 5) 267 (1) 185-91. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United

States. Language: English.

AB The IgE-binding site of the human low-affinity receptor for IgE (Fc epsilon RII/**CD23**) has previously been mapped to the extracellular domain between amino acid residues 160 and 287. We now have investigated which conformational epitope within this domain specifies the receptor-ligand interaction. The analysis of homolog-scanning mutants expressed in mammalian cells demonstrates that amino acid side chains that affect IgE binding are located in two discontinuous segments, between residues 165-190 and 224-256. The overall structure of the **chimeric** binding domains, as probed with 11 conformation-sensitive monoclonal **antibodies**, is generally not distorted, except by replacement of residues 165-183. In this region, disruption of binding function appears to be caused by global conformational constraints on the binding site. Substitution and deletion mutants demonstrate that six out of eight extracellular cysteines, Cys163, Cys174, Cys191, Cys259, Cys273, and Cys282, are necessary for IgE binding and are most likely involved in intramolecular disulfide bridges. We show that the Fc epsilon RII domain delineated by Cys163 and Cys282 encodes all the structural information required to form the IgE-binding site.

L22 ANSWER 34 OF 38 SCISEARCH COPYRIGHT 2003 ISI (R)

92:7051 The Genuine Article (R) Number: GV851. CELL AUTONOMOUS EXPRESSION OF IGD IS NOT ESSENTIAL FOR THE MATURATION OF CONVENTIONAL B-CELLS. ROES J (Reprint); RAJEWSKY K. UNIV COLOGNE, INST GENET, WEYERTAL 121, W-5000 COLOGNE 41, GERMANY (Reprint). INTERNATIONAL IMMUNOLOGY (DEC 1991) Vol. 3, No. 12, pp. 1367-1371. ISSN: 0953-8178. Pub. country: GERMANY. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To analyse the function of IgD in vivo, we generated a 'loss of function' mouse model utilizing gene targeting technology. By homologous recombination in a (C57BL/6 x CBA)F1 mouse embryonic stem cell (ES) line one allele of the delta heavy chain gene was rendered non-functional. In **chimeric** mice obtained after injection of the targeted ES cells into blastocysts derived from severe combined immunodeficient mice we analysed ES cell derived B lymphocytes expressing the targeted or the wild-type allele by using allotype specific reagents. We show that B cells expressing the targeted allele appear in the periphery as IgM+D- cells at normal frequency. They express the **CD23** marker and respond to a T cell dependent antigen. Thus, cell autonomous expression of IgD is neither essential for B cell maturation into an antigen responsive state nor for antigen dependent triggering of the cells into an immune response.

L22 ANSWER 35 OF 38 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 13

91:565320 The Genuine Article (R) Number: GJ565. CHARACTERIZATION OF NEW RAT ANTI-MOUSE IGE MONOCLONALS AND THEIR USE ALONG WITH **CHIMERIC** IGE TO FURTHER DEFINE THE SITE THAT INTERACTS WITH FC-EPSILON-RII AND FC-EPSILON-RI. KEEGAN A D; FRATAZZI C; SHOPES B; BAIRD B; CONRAD D H (Reprint). DEPT MICROBIOL & IMMUNOL, BOX 678, MCV STN, RICHMOND, VA, 23298; STANFORD UNIV, DEPT CELL BIOL, STANFORD, CA, 94305; JOHNS HOPKINS UNIV, GOOD SAMARITAN HOSP, DEPT MED, DIV MOLEC RHEUMATOL, BALTIMORE, MD, 21239; BECTON DICKERSON RES CTR, MT VIEW, CA, 94039; CORNELL UNIV, DEPT CHEM, ITHACA, NY, 14853. MOLECULAR IMMUNOLOGY (1991) Vol. 28, No. 10, pp. 1149-1154. Pub. country: USA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Three rat monoclonal **antibodies** specific for mouse IgE (C12B9, 23G3, and B1E3) were established by using monoclonal anti-DNP mouse IgE (mIgE) as immunogen. These **antibodies**, as well as a fourth, (R1E4) were characterized. It was found that one **antibody** (C12B9) recognizes an allotypic determinant (Igh-7a) found on the C-epsilon chain of mIgE. **Antibody** cross-blocking studies and epitope mapping studies using recombinant mIgE indicated that 3 **antibodies** (C12B9, R1E4 and 23G3) were directed against the

C-epsilon-3 domain while one (B1E3) was directed against the C-epsilon-4 domain. A highly specific sandwich RIA for mIgE was developed using these **antibodies**. Use of these monoclonal anti-mIgE **antibodies** in conjunction with recombinant **chimeric** mIgE-human IgG1 molecules, demonstrated that the C-epsilon-3 domain is important in the binding of mIgE to the murine B cell Fc-epsilon-RII as well as to the murine mast cell Fc-epsilon-RI. The presence of the C-epsilon-4 domain influenced the binding of the recombinant IgE to the Fc-epsilon-RII; in contrast to the C-epsilon-4 domain had no effect on binding to the Fc-epsilon-RI.

L22 ANSWER 36 OF 38 MEDLINE DUPLICATE 14
91191575 Document Number: 91191575. PubMed ID: 1826465. IgE and IgG are synergistic in antigen-mediated release of thromboxane from human lung macrophages. Storch J; MacDermot J. (Department of Clinical Pharmacology, Royal Postgraduate Medical School, London, United Kingdom.) CELLULAR IMMUNOLOGY, (1991 Apr 15) 134 (1) 138-46. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB The mechanism of IgE-mediated release of thromboxane A2 from human lung macrophages has been studied using a monoclonal **chimeric** human/mouse IgE **antibody** and its specific antigen. The cells could be sensitized at 37 degrees C but not at 4 degrees C by incubation with IgE, and released a significant amount of thromboxane A2 (TXA2), measured as the stable hydrolysis product TXB2, in response to an anti-**chimeric** IgE **antibody**. In contrast, stimulation of IgE-sensitized macrophages with the specific antigen produced less than 10% of this response. A similar time course for the release of TXB2 and the formation of inositol monophosphate in the presence of LiCl was observed. Cleavage of the Fc domain of the anti-**chimeric** IgE **antibody** substantially eliminated its capacity to stimulate IgE-sensitized cells. However, the weak or undetectable response to **chimeric** IgE plus specific antigen was substantially potentiated by an antigen-specific **chimeric** IgG **antibody**. IgG-sensitized macrophages did not respond to antigen challenge by the release of TXB2. Preincubation of the cells with a monoclonal **antibody** against the low affinity receptor for IgE (Fc epsilon RII/**CD23**) did not prevent IgE sensitization. We conclude that cell-bound IgE **antibody** cannot induce the release of TXB2 but has fixed antigen which then must interact with specific IgG **antibody** and IgG receptors to induce mediator release.

L22 ANSWER 37 OF 38 MEDLINE DUPLICATE 15
90353389 Document Number: 90353389. PubMed ID: 2167225. IgE-dependent antigen focusing by human B lymphocytes is mediated by the low-affinity receptor for IgE. Pirron U; Schlunck T; Prinz J C; Rieber E P. (Institute for Immunology, University of Munich, FRG.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1990 Jul) 20 (7) 1547-51. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB In this study we investigated the role of the low-affinity receptor for IgE (Fc epsilon RII, **CD23**) on Epstein-Barr virus (EBV)-transformed human B cells in the uptake and presentation to T cells of antigen after complexing with IgE. Cloned EBV-transformed B cells were incubated for 5 h with (4-hydroxy-3-iodo-5-nitrophenyl)acetyl (NIP)-haptenized tetanus toxoid (NIP-TT) or NIP-TT complexed with a **chimeric** human IgE/mouse anti-NIP monoclonal **antibody** (IgE x NIP-TT) and then contacted for 2 min with autologous cloned TT-specific T cells. Intracellular Ca2+ mobilization in T cells was determined as an early indicator of T cell activation. The antigen-presenting capacity of B cells was significantly increased by complexing the antigen with IgE. This effect could be selectively reversed in a dose-dependent manner by blocking the Fc epsilon RII with an anti-**CD23** monoclonal **antibody**. The IgE-mediated

increased capacity for presenting antigen became particularly evident when B cells were incubated with NIP-TT or IgE x NIP-TT for only 1 h at 4 degrees C, washed and then cultivated for 6 h at 37 degrees C allowing uptake and processing of the antigen. These results indicate a new role of the Fc epsilon RII/**CD23** molecules in the uptake of antigen by APC which might be of importance in the maintenance of an ongoing immune response against allergens.

L22 ANSWER 38 OF 38 MEDLINE DUPLICATE 16
90217943 Document Number: 90217943. PubMed ID: 2139100. Expression of the Fc-receptor for IgE (Fc epsilon RII, **CD23**) on alveolar macrophages in extrinsic allergic alveolitis. Pforte A; Breyer G; Prinz J C; Gais P; Burger G; Haussinger K; Rieber E P; Held E; Ziegler-Heitbrock H W. (Medical Department Innenstadt, University of Munich, Federal Republic of Germany.) JOURNAL OF EXPERIMENTAL MEDICINE, (1990 Apr 1) 171 (4) 1163-9. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Expression of the Fc receptor for IgE (Fc epsilon R) was analyzed on alveolar macrophages (AM) in 10 patients with extrinsic allergic alveolitis (EAA) compared with 10 patients with sarcoidosis and to 6 apparently healthy controls. By using the anti-Fc epsilon RII mAb M-L25 in immunocytochemistry experiments, we found that greater than 60% of AM in 10 of 10 patients with EAA were strongly positive, as evidenced by visual analysis in light microscopy and by cytometry. By contrast, no significant staining was detected in sarcoidosis or in controls with either method. Similar results were obtained when Fc epsilon R were identified with preformed immune complexes consisting of NIP-specific human/mouse **chimeric** IgE **antibody** plus NIP-ovalbumin. Furthermore, greater than 60% of AM in patients with EAA stained positive for IgE, demonstrating that endogenous IgE is bound to the AM. Our data suggest that IgE **antibodies** bound to Fc epsilon RII on AM may be involved in pathophysiology of extrinsic allergic alveolitis by activation of the AM after binding of allergen to the cell surface IgE. Furthermore, with the clearcut pattern of Fc epsilon RII expression in extrinsic allergic alveolitis it may be possible to use **CD23** **antibodies** for differential diagnosis of inflammatory lung disease.

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=> dup remove l2
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L23        1353 DUP REMOVE L2 (1947 DUPLICATES REMOVED)

=> s l23 and arthritis
L24         31 L23 AND ARTHRITIS

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L25         31 DUP REMOVE L24 (0 DUPLICATES REMOVED)

=> d l25 1-31 cbib abs

L25 ANSWER 1 OF 31  CAPLUS  COPYRIGHT 2003 ACS
2002:220424  Document No. 136:246408  Combination therapy for treatment of
     autoimmune diseases using B cell depleting/immunoregulatory
     antibody combination..  Hanna, Nabil (Idec Pharmaceuticals, USA).
     PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp.  DESIGNATED STATES: W:
     AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ,
     EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO,
     NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA,
     GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).
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CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L25 ANSWER 2 OF 31 MEDLINE

2002012311 Document Number: 21302711. PubMed ID: 11409113. Mechanisms of **CD23** hyperexpression on B cells from patients with rheumatoid **arthritis**. De Miguel S; Galocha B; Jover J A; Banares A; Hernandez-Garcia C; Garcia-Asenjo J A; Fernandez-Gutierrez B. (Services of Rheumatology and Pathology, Hospital Clinico San Carlos, Madrid, Spain.) JOURNAL OF RHEUMATOLOGY, (2001 Jun) 28 (6) 1222-8. Journal code: 7501984. ISSN: 0315-162X. Pub. country: Canada. Language: English.

AB OBJECTIVE: To analyze the mechanisms involved in the characteristic hyperexpression of **CD23** on peripheral blood B cells from patients with rheumatoid **arthritis** (RA). METHODS: Peripheral blood mononuclear cells (PBMC) were obtained from patients with active disease and activated during 18 h with an anti-CD3 monoclonal **antibody** in the presence or absence of blocking **antibodies** to CD154 or CD40. PBMC were further purified by rosetting and **CD23** expression was assessed on B cells by flow cytometry after double staining (CD19/**CD23**). Lymphocytes were also isolated from synovial fluid (SF). CD154 expression was analyzed on PB or SF CD4+ T cells after double staining (CD4/CD154) by flow cytometry at basal conditions and after different stimuli [anti-CD3 or phorbol myristic acetate (PMA) plus ionomycin]. Co-culture experiments between SF and PB cells were performed to analyze the involvement of the CD40-CD154 interaction on **CD23** expression. CD154 and **CD23** expression was also analyzed on synovial membrane by immunohistochemical techniques. RESULTS: A high proportion of activated **CD23** B cells was detected in patients with RA. Blocking experiments with both anti-CD40 and anti-CD154 Mab showed a significant reduction in the proportion of PB B cells expressing **CD23**. Following activation with anti-CD3 Mab or PMA plus ionomycin, CD154 expression was mainly induced on PB CD4+ T cells. In co-culture experiments, SF T cells were more efficient than PB T cells in inducing CD40 dependent **CD23** expression on PB B cells. In addition, CD4+ T cells from synovial membrane clearly expressed CD154. CONCLUSION: Our results establish a link between CD154-CD40 pathway and **CD23** expression on PB B cells from patients with RA. T cells from the synovial microenvironment were active participants in this **CD23** expression, presumably in the context of cell recirculation.

L25 ANSWER 3 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

2001299562 EMBASE Lymphoma in a patient with rheumatoid **arthritis** receiving methotrexate treatment: Successful treatment with rituximab. Stewart M.; Malkovska V.; Krishnan J.; Lessin L.; Barth W.. Dr. W. Barth, 2021 K Street, NW, Washington, DC 20006, United States. wfbarth@worldnet.att.net. Annals of the Rheumatic Diseases 60/9 (892-893) 2001.

Refs: 18.

ISSN: 0003-4967. CODEN: ARDIAO. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB A 55 year old man with chronic lymphocytic leukaemia (CLL) and rheumatoid **arthritis** (RA), treated for four years with methotrexate (MTX), who developed a B cell non-Hodgkin's lymphoma (B-NHL), is described. The tumour was localised to the shoulder and axillary lymph nodes, and positive for Epstein-Barr viral antigens. After failure of radiation and chemotherapy, a complete remission was achieved with a combination of

antibody treatment (rituximab) and EPOCH. The development of a second malignancy in a patient with RA receiving MTX has not been described before. The summation of T cell deficiencies induced by MTX, CLL, and RA may all have contributed to the development of the B-NHL.

L25 ANSWER 4 OF 31 SCISEARCH COPYRIGHT 2003 ISI (R)
2001:404948 The Genuine Article (R) Number: 431CQ. Anti-interleukin-1 therapy in rheumatic diseases. Dayer J M (Reprint); Feige U; Edwards C K; Burger D. Univ Hosp Geneva, Div Immunol & Allergy, CH-1211 Geneva 14, Switzerland (Reprint); Amgen Inc, Dept Pharmacol, Thousand Oaks, CA 91320 USA; Amgen Inc, Dept Inflammat Res, Thousand Oaks, CA 91320 USA. CURRENT OPINION IN RHEUMATOLOGY (MAY 2001) Vol. 13, No. 3, pp. 170-176. Publisher: LIPPINCOTT WILLIAMS & WILKINS. 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA. ISSN: 1040-8711. Pub. country: Switzerland; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Recent research has shown that in the processes of rheumatoid **arthritis** (RA), interleukin (IL)-1 is one of the pivotal cytokines in initiating disease, and the body's natural response, IL-1 receptor antagonist (IL-1 Ra), has been shown conclusively to block its effects. In laboratory and animal studies inhibition of IL-1 by either **antibodies** to IL-1 or IL-1 Ra proved beneficial to the outcome. To date, two large well-controlled studies in patients with RA led to the conclusion that IL-1 Ra is clinically effective and that it slows progression of bone damage as measured radiographically. Being a specific, selective inhibitor of the IL-1 pathway, IL-1 Ra could constitute an important new approach to treating patients with RA that significantly reduces the signs and symptoms of the disease, reduces joint destruction and up to now has proved Safe and well tolerated. (C) 2001 Lippincott Williams & Wilkins, Inc.

L25 ANSWER 5 OF 31 SCISEARCH COPYRIGHT 2003 ISI (R)
2001:645316 The Genuine Article (R) Number: 460PV. Proteases produced by activated neutrophils release soluble **CD23** fragments endowed with proinflammatory effects. Brignone C; Munoz O; Batoz M; Rouquette-Jazdanian A; Cousin J L (Reprint). Hop Archet, INSERM, U343, BP 79, F-06202 Nice 3, France (Reprint); Hop Archet, INSERM, U343, F-06202 Nice 3, France; Dana Farber Canc Inst, Boston, MA 02115 USA. FASEB JOURNAL (JUL 2001) Vol. 15, No. 9, pp. U80-U100. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. ISSN: 0892-6638. Pub. country: France; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Polymorphonuclear neutrophils (PMNs) are the major source of proteolytic activities involved mainly in tissue injuries observed in chronic inflammatory disorders. High levels of soluble forms of **CD23** (the low-affinity receptor for IgE) were found in biological fluids from these patients, and recent reports focused on a **CD23** -mediated regulation of inflammatory response. In this context, we show here that co-culture of activated PMN with **CD23**(+) B cells resulted in a drastic release of soluble **CD23** fragments from the cell surface. This cleavage was inhibited by serine proteases inhibitors, including alpha1-antitrypsin. We next demonstrated that purified human leukocyte elastase or cathepsin G efficiently cleaved membrane **CD23** on B cells with a high specificity. Soluble fragments released by serine proteases-mediated **CD23** proteolysis stimulated resting monocytes to produce oxidative burst and proinflammatory cytokine without any co-stimulatory signal. This work strongly supports the idea that the capacity of PMN-derived proteases to release soluble forms of **CD23** participates in the inflammatory process mediated by these cells.

L25 ANSWER 6 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2001010066 EMBASE Increased expression of **CD23** in rheumatoid synovitis. Huissoon A.P.; Emery P.; Bacon P.A.; Gordon J.; Salmon M.. M.

Salmon, Department of Rheumatology, Medical School, University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom. m.salmon@bham.ac.uk. Scandinavian Journal of Rheumatology 29/3 (154-159) 2000.
Refs: 22.
ISSN: 0300-9742. CODEN: SJRHAT. Pub. Country: Norway. Language: English. Summary Language: English.

AB Objective. Soluble (s)**CD23** is a potent macrophage stimulator. High levels of this molecule have been reported in rheumatoid **arthritis** (RA) serum. We investigated the expression of **CD23** and its ligands in rheumatoid synovial fluid and cells. Methods. Levels of sCD23, and cellular expression of **CD23** and its ligands CD21, CD11b, and CD11c were measured in synovial fluid (SF) of RA patients and in blood of RA patients and controls. Results. SF contained higher levels of sCD23 than either rheumatoid or normal sera (median 4.8, 3.16, and 1.13 ng/ml respectively, $p<0.01$). Synovial **CD23** was found to be expressed principally on macrophages. While little CD21 expression was detected, CD11b and CD11c were both expressed at high levels, particularly on macrophages. Conclusions. Soluble **CD23** is present in high levels in RA synovial fluid. Macrophages appear to be the principal source. Macrophages also express ligands for sCD23, and may therefore also be the targets of this potent pro-inflammatory molecule.

L25 ANSWER 7 OF 31 SCISEARCH COPYRIGHT 2003 ISI (R)

1999:673451 The Genuine Article (R) Number: 230LJ. Absence of demonstrable immune dysregulation in motor neuron disease. Bansal A S (Reprint); Bansal J A; Bruce J; Boyle R. ST HELIER HOSP, WRYTHE LANE, CARSHALTON SM5 1AA, SURREY, ENGLAND (Reprint); UNIV QUEENSLAND, PRINCESS ALEXANDRA HOSP, DEPT MED, BRISBANE, QLD 4102, AUSTRALIA; QUEENSLAND UNIV TECHNOL, FAC HLTH, BRISBANE, QLD 4059, AUSTRALIA; PRINCESS ALEXANDRA HOSP, LIONS HUMAN IMMUNOL LAB, BRISBANE, QLD 4102, AUSTRALIA. JOURNAL OF CLINICAL NEUROSCIENCE (JUL 1999) Vol. 6, No. 4, pp. 309-312. Publisher: CHURCHILL LIVINGSTONE. JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND. ISSN: 0967-5868. Pub. country: ENGLAND; AUSTRALIA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Patients with motor neuron disease (MND) (n=33) free of infection were assessed for symptoms of autoimmunity and evidence of peripheral immune activation. Clinical features of autoimmune disease and antinuclear **antibodies** were notably absent in all patients. Compared with healthy controls, patients with MND had no significant difference in lymphocyte subsets (CD4/8 T cells, B and NK cells). Serum and whole blood endotoxin and phytohaemagglutinin stimulated levels of interferon gamma, granulocyte macrophage colony stimulating factor, interleukin (IL) 1 beta, IL4, IL10, tumour necrosis factor alpha and soluble **CD23** were no different between patients with MND and healthy controls. Our results confirm the absence of significant elevations of immune regulatory proteins in the peripheral circulation of patients with MND.

L25 ANSWER 8 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

1999401356 EMBASE [Contribution of some laboratory examinations to the diagnosis and evaluation of rheumatoid **arthritis**]. PRINOS NEKTERYCH LABORATORNICH VYSETRENI K DIAGNOSTICE A HODNOCENI REVMATOIDNI ARTRITIDY. Vencovsky J.; Pesakova V.; Kafkova J.; Cimburek Z.; Haiselova L.; Sedova L.; Ruzickova S.. Dr. J. Vencovsky, Revmatologicky Ustav, Na slupi 4, 128 50 Praha 2, Czech Republic. Ceska Revmatologie 7/4 (155-165) 1999.
Refs: 70.
ISSN: 1210-7905. CODEN: CRVMEG. Pub. Country: Czech Republic. Language: Czech. Summary Language: English; Czech.

AB Objective: To assess the contribution of selected laboratory examinations to the diagnosis and evaluation of patients with rheumatoid

arthritis (RA). Patients and methods: In 115 patients with RA, 86 healthy controls and in 110 patients with systemic autoimmune diseases the authors examined antikeratin **antibodies** (AKA) and antiperinuclear **antibodies** (APF) by indirect immunofluorescence, isotypes of rheumatoid factors by the ELISA method and anti-RA33 **antibodies** by immunoblotting on the semipurified extract. The HLA-DR status of the patients was assessed and subtyping of the HLA-DRB1*04 alleles was performed. AKA were assessed also in synovial fluid of 24 patients with RA and 31 patients with knee osteoarthritis. Finally also the serum level of **CD23** molecules was assessed in 30 patients and healthy controls. Results: Positive results in RA were proved for RF in 75.6%, for APF in 52.2%, for AKA in 39%, for anti-RA33 in 17.4%. In healthy controls RF were present in 5.8%; AKA, APF and anti-RA33 were practically not detected. The 'shared epitope' was found in 69.6% patients, while only in 32.5% healthy subjects ($p<0.001$). Correlation with the clinical condition and CRP level revealed an association only with activity and APF or anti-RA33 and RF and the severity of RA. Carriers of the 'shared epitope' have more frequently a positive APF. The sCD23 levels are slightly elevated in RA (6.18 ng/ml), unrelated to the clinical status. Conclusion: RF are the most frequent **antibodies** in RA but the specificity of the examination is not sufficient. In RF negative cases or for confirmation of the diagnosis the assessment of APF or AKA may be useful. Some correlations with the clinical status may contribute to a better evaluation of the activity or severity of RA. There is only a slight predisposition for the formation of autoantibodies in patients with RA having HLA alleles with the 'shared epitope'.

L25 ANSWER 9 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

1999094239 EMBASE [IgE containing immune complexes in serum and synovial fluid from patients with rheumatoid **arthritis**]. IGE-HALTIGE IMMUNKOMPLEXE IM SERUM UND IN DER SYNOVIALFLUSSIGKEIT YON PATIENTEN MIT RHEUMATOIDER **ARTHRITIS**. Lossner M.; Hein G.; Herrmann D.. Dr. D. Herrmann, Institut fur Klinische Immunologie, Klin. der Friedrich-Schiller-Univ., Am Johannisfriedhof 3, D-07740 Jena, Germany. Allergologie 22/2 (113-118) 1999.
Refs: 23.
ISSN: 0344-5062. CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: English; German.

AB Circulating immune complexes in patients with rheumatoid **arthritis** (RA) are composed of the immunoglobulins M and G, less frequent also A and E, and complement components. For determination IgE containing complexes (IK-E) are precipitated by polyethylene glycol 6,000, 2.5% in PBS. After extensive washing, the precipitate is solubilised in PBS and the IgE content measured by enzyme immunoassay. IK-E have been found in 3 sera out of 92 healthy donors (3%), in 43 out of 101 patients suffering from RA (43%), in 36 out of 83 patient with atopic dermatitis (43%), and 4 out of 50 patients with psoriasis vulgaris (8%). In 20 synovial fluids from RA patients, IK-E have been measured, too. The results obtained in sera and in synovial fluids are correlating. Patients, suffering less than 20 years from RA and having IK-E in serum, show a significantly higher restriction of mobility, measured by the mobility function test by Keitel, than patients without such complexes. After longer duration of the disease, these differences seem to disappear. For a precise statement, the number of patients suffering from RA longer than 20 years is to small. Circulating immune complexes have been measured too (C1q-binding test, not determining any immune globulin class). There was no difference between groups of patients with and without such complexes. Therefore, IK-E can be used as markers of a more severe disease. It can be assumed, that such complexes activate, or increase activation of cells expressing high-affinity IgE receptors, such as mast cells, and low affinity receptors (**CD23**), such as macrophages. Thus, the inflammation could be increased by IK-E.

L25 ANSWER 10 OF 31 MEDLINE

1999049828 Document Number: 99049828. PubMed ID: 9834082. Inhibitors of the p38 mitogen-activated kinase modulate IL-4 induction of low affinity IgE receptor (**CD23**) in human monocytes. Marshall L A; Hansbury M J; Bolognese B J; Gum R J; Young P R; Mayer R J. (Department of Immunopharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406, USA.) JOURNAL OF IMMUNOLOGY, (1998 Dec 1) 161 (11) 6005-13. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB **CD23**, the low affinity IgE receptor, is up-regulated on the surface of IL-4-treated B cells and monocytes and is immediately proteolytically processed, releasing soluble fragments of **CD23**. Here, we report that inhibitors of the p38 mitogen-activated kinase (p38 MAPK), SK&F 86002 or the more selective inhibitor, SB 203580, reduce the levels of soluble **CD23** formed by IL-4-stimulated human monocytes or the human monocytic cell line, U937. In contrast to compounds such as the metalloprotease inhibitor batimastat ([4-(N-hydroxyamino)-2-(R)-isobutyl-3-(S)-(2-thiophenethiomethyl)s uccinyl]-(S)-phenylalanine-N-methylamide, sodium salt), p38 MAPK inhibitors do not directly inhibit proteolytic processing of **CD23**. Further, evaluation of surface intact **CD23** (iCD23) by flow cytometry demonstrated that SK&F 86002 and SB 203580 reduced the surface expression of iCD23 in a concentration-dependent fashion, while batimastat increased the surface expression of iCD23. The decrease in surface iCD23 was accompanied by a decrease in total cell-associated **CD23** protein levels but not **CD23** mRNA. IL-4 induced a late (>4-h) increase in p38 MAPK activity and corresponding activation of its substrate MAPKAPK-2. This activation was blocked by addition of SB 203580 before IL-4 induction, in parallel with the inhibition of **CD23** expression. Modulation of **CD23** by **antibodies** has been shown to alleviate the symptoms of murine collagen-induced **arthritis**, implicating **CD23** as an important proinflammatory agent. These data show that in addition to the known cytokine inhibitory actions of SK&F 86002 and SB 203580, they also confer an additional potential anti-inflammatory activity through modulation of **CD23** expression.

L25 ANSWER 11 OF 31 MEDLINE

1998452349 Document Number: 98452349. PubMed ID: 9779313. Serum soluble **CD23** levels and **CD23** expression on peripheral blood mononuclear cells in juvenile chronic **arthritis**. Massa M; Pignatti P; Oliveri M; De Amici M; De Benedetti F; Martini A. (Laboratorio Biotecnologie e Tecnologie Biomediche, Universita degli Studi di Pavia, I.R.C.C.S. Policlinico San Matteo, Italy.) CLINICAL AND EXPERIMENTAL RHEUMATOLOGY, (1998 Sep-Oct) 16 (5) 611-6. Journal code: 8308521. ISSN: 0392-856X. Pub. country: Italy. Language: English.

AB OBJECTIVE: To assess the **CD23** status in patients with juvenile chronic **arthritis** (JCA), as defined by serum soluble **CD23** (sCD23) and the expression of **CD23** on peripheral blood mononuclear cells. METHODS: Serum sCD23 levels were measured by ELISA in 22 patients with systemic JCA (s-JCA), in 40 patients with antinuclear **antibody** positive pauciarticular JCA (ANA+ p-JCA), and in 38 healthy controls. **CD23** expression on T cells, B cells, and monocytes was determined by flow cytometry analysis of double fluorescence staining. RESULTS: Serum sCD23 levels were increased in both ANA+ p-JCA and s-JCA; no relation with disease activity or severity was found. In patients with ANA+ p-JCA, serum sCD23 levels were correlated with an increased percentage of B cells expressing **CD23**, while in patients with s-JCA the serum sCD23 levels were correlated with an increased percentage of monocytes expressing **CD23**. CONCLUSION: Serum sCD23 levels are elevated both in systemic and ANA+ pauciarticular JCA: different cell subset **CD23** expression in s-JCA and ANA+ p-JCA (i.e. monocyte or B cell, respectively) suggests that in pauciarticular JCA **CD23** may be implicated in B cell activation

and autoantibody production, while in systemic JCA may be involved in monocyte activation and in the release of inflammatory mediators.

L25 ANSWER 12 OF 31 MEDLINE
1998000978 Document Number: 98000978. PubMed ID: 9341771. Mouse **CD23** regulates monocyte activation through an interaction with the adhesion molecule CD11b/CD18. Lecoanet-Henchoz S; Plater-Zyberk C; Graber P; Gretener D; Aubry J P; Conrad D H; Bonnefoy J Y. (Geneva Biomedical Research Institute, Glaxo Wellcome Research and Development, Switzerland.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Sep) 27 (9) 2290-4. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB **CD23** is expressed on a variety of hemopoietic cells. Recently, we have reported that blocking **CD23** interactions in a murine model of **arthritis** resulted in a marked improvement of disease severity. Here, we demonstrate that CD11b, the alpha chain of the beta 2 integrin adhesion molecule complex CD11b/CD18 expressed on monocytes interacts with **CD23**. Using a recombinant fusion protein (ZZ-**CD23**), murine **CD23** was shown to bind to peritoneal macrophages and peripheral blood cells isolated from mice as well as the murine macrophage cell line, RAW. The interactions between mouse ZZ-**CD23** and CD11b/CD18-expressing cells were significantly inhibited by anti-CD11b monoclonal **antibodies**. A functional consequence was then demonstrated by inducing an up-regulation of interleukin-6 (IL-6) production following ZZ-**CD23** incubation with monocytes. The addition of Fab fragments generated from the monoclonal **antibody** CD11b impaired this cytokine production by 50%. Interestingly, a positive autocrine loop was identified as IL-6 was shown to increase **CD23** binding to macrophages. These results demonstrate that similar to findings using human cells, murine **CD23** binds to the surface adhesion molecule, CD11b, and these interactions regulate biological activities of murine myeloid cells.

L25 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2003 ACS
1997:353668 Document No. 127:16300 Clinical significance of soluble CD4, CD8, **CD23** molecules in rheumatic diseases. Sawada, Shigemasa (Sch. Med., Nihon Univ., Tokyo, 179, Japan). Nichidai Igaku Zasshi, 56(3), 114-116 (Japanese) 1997. CODEN: NICHAS. ISSN: 0029-0424. Publisher: Nihon Daigaku Igakkai.

AB A review with 16 refs. Changes in the serum levels of sol. forms of CD4, CD8 and **CD23** (sCD4, sCD8, sCD23) are reported in human autoimmune diseases. SCD4 level increases and sCD8 level decreases in primary Sjoegren's syndrome, and the levels are comparable to normal subjects in secondary Sjoegren's syndrome. Serum IgG level strongly correlates with sCD4 level. SCD4 and sCD8 levels increase in systemic lupus erythematosus (SLE). SCD4 level correlates with serum IgG level, esp. with anti-DNA **antibody** level and not with the other autoimmune **antibody** levels as anti-ribonucleoprotein (RNP) **antibody**. SCD4 level correlates with serum complement level, and sCD8 correlates with erythrocyte sedimentation rate (ESR). SCD4, sCD8 and sCD23 levels increase in rheumatoid **arthritis** (RA). SCD8 level correlates with ESR and C-reactive protein (CRP) level. sCD23 level correlates with ESR, CRP and rheumatoid factor level. abs; sCD8 level increases in acute virus infection, and chronic elevation of sCD4 level suggests human immunodeficiency virus (HIV) infection or HIV-related retrovirus infection.

L25 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE,

KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L25 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2003 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative treatment of mice against **arthritis** using monoclonal anti-**CD23 antibody, CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L25 ANSWER 16 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

96303695 EMBASE Document No.: 1996303695. The presence of interleukin-13 in rheumatoid synovium and its antiinflammatory effects on synovial fluid macrophages from patients with rheumatoid **arthritis**. Isomaki P.; Luukkainen R.; Toivanen P.; Punnonen J.. Department of Medical Microbiology, Turku University, Kiinamyllynkatu 13,FIN-20520 Turku, Finland. Arthritis and Rheumatism 39/10 (1693-1702) 1996. ISSN: 0004-3591. CODEN: ARHEAW. Pub. Country: United States. Language: English. Summary Language: English.

AB Objective. To study the production of interleukin-13 (IL-13) in rheumatoid synovium and the effects of recombinant IL-13 on the phenotype and function of synovial fluid (SF) macrophages and T cells derived from patients with rheumatoid **arthritis** (RA). Methods. The presence of IL-13 in SF was studied using an IL-13-specific enzyme-linked immunosorbent assay (ELISA); the production of IL-13 was studied in SF mononuclear cells (SFMC) by reverse transcriptase-polymerase chain reaction. The effects of recombinant IL-13 on cytokine production by and phenotype of SFMC were evaluated using cytokine- specific ELISAs and flow cytometry, respectively. The effect of IL-13 on the proliferation of SFMC was determined by 3H-thymidine incorporation. The production and the effects of IL-13 were compared with those of IL-4. Results. IL-13 was

present in 27 of 28 SF samples, and IL-13 messenger RNA (mRNA) was detectable in SFMC. Importantly, IL-13 levels were significantly higher than those of IL-4, and IL-13 protein and mRNA were expressed in several samples, although IL-4 synthesis was undetectable. Recombinant IL-13 significantly reduced the production of IL-1.beta. and tumor necrosis factor a and the expression of CD16 and CD64 by SF macrophages, whereas the expression of HLA-DR and **CD23** was increased. These effects on SF macrophages were similar to those observed with IL-4, but in contrast to IL-4, IL-13 had no growth-promoting effect on SF T cells. Conclusion. IL-13 is consistently present in rheumatoid synovium. The ability of exogenous IL-13 to decrease the production of proinflammatory cytokines by SFMC suggests that it may have therapeutic potential in the treatment of patients with RA.

L25 ANSWER 17 OF 31 MEDLINE
97007284 Document Number: 97007284. PubMed ID: 8854559. A new role for **CD23** in inflammation. Bonnefoy J Y; Plater-Zyberk C; Lecoanet-Henchoz S; Gauchat J F; Aubry J P; Graber P. (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland.. JYB2300@GGR.CO.UK) . IMMUNOLOGY TODAY, (1996 Sep) 17 (9) 418-20. Journal code: 8008346. ISSN: 0167-5699. Pub. country: ENGLAND: United Kingdom. Language: English.

L25 ANSWER 18 OF 31 SCISEARCH COPYRIGHT 2003 ISI (R)
96:759060 The Genuine Article (R) Number: VL947. ELEVATED LEVELS OF SOLUBLE FC-EPSILON-RII/**CD23** AND **ANTIBODIES** TO EPSTEIN-BARR-VIRUS IN PATIENTS WITH SJOGRENS-SYNDROME. SUZUKI M (Reprint); NAGATA S; HIRAMATSU K; TAKAGI I; ITO H; KITAO S; ITO M; OHTA N; BABA S. NAGOYA CITY UNIV, SCH MED, DEPT OTORHINOLARYNGOL, MIZUHO KU, 1 KAWASUMI, NAGOYA, AICHI 467, JAPAN (Reprint); NAGOYA CITY UNIV, SCH MED, DEPT MED ZOOL, NAGOYA, AICHI 467, JAPAN. ACTA OTO-LARYNGOLOGICA (1996) Supp. 525, pp. 108-112. ISSN: 0001-6489. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB To clarify how Epstein-Barr virus (EBV) infection is responsible for Sjogren's syndrome (SjS) we measured both IgG and IgM **antibodies** to viral capsid antigen (VCA) of EBV in the sera of normal healthy subjects and patients with SjS. Anti-VCA IgG was detectable in all controls and patients; however, anti-VCA IgG titers in the sera of SjS patients were significantly higher than those of the controls ($p < 0.01$). No anti-VCA IgM was detected in the sera of controls whereas anti-VCA IgM was detected in the sera from 10 out of the 13 patients with SjS. This suggests that SjS might be associated with EBV. The serum levels of sCD23 (IgE-binding factor) were also measured to assess the differential state in patients with SjS. The sCD23 level of normal individuals was 211.26+/-12.01 mu g/L (value is mean+/-SE), and was 443.77+/-71.94 mu g/L in the 13 patients with SjS The mean sCD23 level in the 9 patients with SjS without any complication was 360.67+/-35.63 mu g/L. In the patients with SjS, sCD23 levels were significantly higher than those in the normal individuals ($p < 0.01$).

L25 ANSWER 19 OF 31 SCISEARCH COPYRIGHT 2003 ISI (R)
95:735643 The Genuine Article (R) Number: RX684. TREATMENT WITH **ANTIBODIES** TO **CD23** MARKEDLY AMELIORATES AN ESTABLISHED COLLAGEN-INDUCED **ARTHRITIS** IN MICE. PLATERZYBERK C (Reprint); BONNEFOY J Y. GLAXO IMB, DEPT IMMUNOL, CH-1228 GENEVA, SWITZERLAND. ARTHRITIS AND RHEUMATISM (SEP 1995) Vol. 38, No. 9, Supp. S, pp. 942. ISSN: 0004-3591. Pub. country: SWITZERLAND. Language: ENGLISH.

L25 ANSWER 20 OF 31 MEDLINE
96071560 Document Number: 96071560. PubMed ID: 7585180. Marked amelioration of established collagen-induced **arthritis** by treatment with **antibodies** to **CD23** in vivo.

Plater-Zyberk C; Bonnefoy J Y. (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland.) NATURE MEDICINE, (1995 Aug) 1 (8) 781-5. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB **CD23** is a low-affinity receptor for immunoglobulin E (IgE) expressed by a variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. **CD23** regulates many functional aspects of immune cells, both in its cell-associated and soluble forms. In view of the increased levels of **CD23** in rheumatoid **arthritis**, we have studied the effect of neutralizing **CD23** in type II collagen-induced **arthritis** in mice, a model for human rheumatoid **arthritis**. Successful disease modulation is achieved by treatment of arthritic DBA/1 mice with either polyclonal or monoclonal **antibodies** to mouse **CD23**. Treated mice show a dose-related amelioration of **arthritis** with significantly reduced clinical scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decrease in cellular infiltration of the synovial sublining layer and limited destruction of cartilage and bone is evident in animals treated with therapeutic doses of anti-**CD23** **antibody**. These findings demonstrate the involvement of **CD23** in a mouse model of human rheumatoid **arthritis**.

L25 ANSWER 21 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

1995:521449 Document No.: PREV199598535749. Treatment with **antibodies** to **CD23** markedly ameliorates an established collagen-induced **arthritis** in mice. Plater-Zyberk, Christine; Bonnefoy, Jean-Yves. Glaxo IMB, Immunol. Dep., 14 Chemin Des Aulx, CH-1228 Geneva Switzerland. Arthritis & Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S310. Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals San Francisco, California, USA October 21-26, 1995 ISSN: 0004-3591. Language: English.

L25 ANSWER 22 OF 31 MEDLINE

94340805 Document Number: 94340805. PubMed ID: 8062447. **CD23** hyperexpression in rheumatoid **arthritis**: evidence for a B cell hyperresponsiveness to cognate and noncognate T-cell signals. Fernandez-Gutierrez B; Hernandez-Garcia C; Banares A A; Jover J A. (Rheumatology Service, Hospital Universitario San Carlos, Madrid, Spain.) CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1994 Sep) 72 (3) 321-7. Journal code: 0356637. ISSN: 0090-1229. Pub. country: United States. Language: English.

AB We have studied the causes of membrane **CD23** (mCD23) hyperexpression in rheumatoid **arthritis** (RA). Modifying a previously developed in vitro system, we cultured RA and control peripheral blood (PB) mononuclear cells for 18 hr with medium, anti-CD3 monoclonal **antibody** (mAb), recombinant (r) IL-4, or phorbol myristate acetate (PMA). After T cell depletion by rosetting, mCD23 was assessed by indirect immunofluorescence. RA PB B cells expressed mCD23 in a percentage significantly higher than controls unstimulated (16.7% vs. 6.6%) and after culture with anti-CD3-stimulated T cells (53% vs. 37.2%) or IL-4 (47% vs. 30%), but not after PMA (37.5% vs. 31%). We did not see differences in the percentages of resting B cells between RA and controls. Our results show an intrinsic RA PB B cell hyperesponsiveness to different T cell signals that might be mediated by in vivo priming through surface immunoglobulin.

L25 ANSWER 23 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

94160633 EMBASE Document No.: 1994160633. Increased levels of sCD23 in rheumatoid **arthritis** are related to disease status. Bansal A.S.; MacGregor A.J.; Pumphrey R.S.H.; Silman A.J.; Ollier W.E.R.; Wilson P.B..

Regional Immunology Department, St. Mary's Hospital, Hathersage Road,Manchester M13 0JH, United Kingdom. Clinical and Experimental Rheumatology 12/3 (281-285) 1994.
ISSN: 0392-856X. CODEN: CERHDP. Pub. Country: Italy. Language: English. Summary Language: English.

AB The low affinity receptor for IgE (Fc.epsilon.RII, **CD23**) is involved in many aspects of T and B cell regulation. In the current study, serum levels of sCD23 were measured in monozygotic (MZ) twins discordant for rheumatoid **arthritis** (RA) to examine whether an increased level of sCD23 in RA is, at least in part, genetically determined. Paired analysis showed significantly elevated sCD23 levels in affected twins when compared with their unaffected co-twins ($p < 0.01$). There was no significant difference in sCD23 in the unaffected twins compared with normal controls. Higher levels of sCD23 were found in males compared to females in both affected and unaffected twins. Soluble **CD23** showed a significant increase with age in RA affected twins ($p = 0.013$), but no association with disease duration ($p = 0.87$). There was no significant variation in sCD23 level with HLA-DR phenotype. We conclude that elevations in serum sCD23 in patients with RA are primarily disease related.

L25 ANSWER 24 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

94084024 EMBASE Document No.: 1994084024. Soluble Fc.epsilon.RII/**CD23** in patients with autoimmune diseases and Epstein-Barr virus-related disorders: Analysis by ELISA for soluble Fc.epsilon.RII/**CD23**.
Yoshikawa T.; Nanba T.; Kato H.; Hori K.; Inamoto T.; Kumagai S.; Yodoi J.. Department of Biological Responses, Institute for Virus Research, Kyoto University, 53 Shogoin-Kawahara-cho,Sakyo, Kyoto 606-01, Japan.
ImmunoMethods 4/1 (65-71) 1994.
ISSN: 1058-6687. CODEN: IMUME8. Pub. Country: United States. Language: English. Summary Language: English.

AB The low-affinity Fc receptor for IgE (Fc.epsilon.RII/**CD23**) and its soluble form (sCD23, IgE-binding factor) have multiple functions, and enhanced levels of these are associated with various immunological diseases. We established two sensitive ELISA systems using enzyme-conjugated mAb and biotinylated mAb. The detection limits of the ELISA systems were 0.03 and 1.0 ng/ml, which showed good correlation in the range 1.0-10 ng/ml. In the ELISA system using enzyme-conjugated mAb, the average sCD23 concentration in 303 normal healthy volunteers was 1.4 .+-. 0.3 ng/ml. In the ELISA system using biotinylated mAb, sCD23 levels in normal healthy volunteers showed almost the same values. In patients with autoimmune diseases such as rheumatoid **arthritis**, systemic lupus erythematosus, Sjogren syndrome, progressive systemic sclerosis, and mixed connective tissue disease, the sCD23 levels were significantly higher than those in normal individuals. Furthermore, in Epstein-Barr virus-related disorders after liver transplantation with immunosuppression, plasma levels of sCD23 rapidly increased to more than 12 ng/ml when clinical symptoms were evident. In addition, the sCD23 values remained high, although elevated GOT levels gradually decreased to standard values and EBV hepatitis improved. These data suggest that sCD23 levels are a sensitive marker of autoimmune diseases and EBV-related disorders in addition to allergic disorders. The ELISA system for sCD23 may be an additional diagnostic tool in estimating the clinical courses of these diseases.

L25 ANSWER 25 OF 31 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

1993:523474 Document No.: PREV199396136881. Synovial fluid macrophages and blood monocytes differ in their responses to IL-4. Hart, Prue H. (1); Ahern, Michael J.; Jones, Catherine A.; Jones, Kristen L.; Smith, Malcolm D.; Finlay-Jones, John J.. (1) Dep. Microbiol. Infectious Diseases, Sch. Med., Flinders University South Australia, GPO Box 2100, Adelaide, Aust. 5001. Journal of Immunology, (1993) Vol. 151, No. 6, pp. 3370-3380. ISSN: 0022-1767. Language: English.

AB IL-4 has been described as a potential anti-inflammatory molecule because of its ability in vitro to down-regulate human monocyte production of proinflammatory mediators. In this study, the activity of IL-4 on mononuclear cells and CD14+ macrophages from a site of chronic inflammation, namely, the joints of patients with rheumatoid and psoriatic **arthritis**, was investigated and compared directly with its activity on PBMC and monocytes from the same patients. In contrast to the response by blood monocytes, the response to IL-4 by synovial fluid cells was selective; IL-4 did not significantly suppress LPS-induced TNF-alpha production, but decreased CD14 expression to a similar extent in the two cell populations. IL-4 induction of monocyte/macrophage **CD23** expression was investigated as a stimulatory response to IL-4, and although significantly increased on synovial fluid CD14+ cells by IL-4, the induction was considerably reduced compared with that measured for blood cells. Activation and differentiation in vitro of blood monocytes reduced their response to IL-4 for decreased TNF-alpha production and induction of **CD23** and suggested that these biologic phenomena may contribute to the decreased responsiveness to IL-4 by synovial fluid monocytes/macrophages. Thus, IL-4 does not have the same anti-inflammatory properties in vitro on synovial fluid cells as on blood monocytes.

L25 ANSWER 26 OF 31 MEDLINE

93357689 Document Number: 93357689. PubMed ID: 7689005. Possible role of CD5+ B cells expressing **CD23** in mediating the elevation of serum-soluble **CD23** in patients with rheumatoid **arthritis** . Ikizawa K; Yanagihara Y; Kajiwara K; Koshio T; Shida T; Yamada A. (Clinical Research Center for Allergy, National Sagamihara Hospital, Japan.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1993) 101 (4) 416-24. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB Since increased levels of serum soluble **CD23**/Fc epsilon RII (sCD23) were evidently demonstrated in patients with autoimmune diseases such as rheumatoid **arthritis** (RA), the possible mechanisms responsible for the elevation of serum sCD23 were investigated in RA patients. In keeping with increased serum sCD23, high proportion of **CD23**+ B cells was detected in the patients; this was associated with the enhanced expression of only Fc epsilon RIIa mRNA. Upon incubation at 37 degrees C, peripheral blood mononuclear cells of the patients spontaneously released high levels of sCD23 into the culture supernatant, while the **CD23** expression on their B cells was considerably maintained even after the culture. Dot blot analysis further revealed that in contrast to normal subjects, RA patients showed no complete disappearance of Fc epsilon RIIa mRNA after the spontaneous culture. In addition, sCD23 release was significantly reduced in the patients by the addition of cycloheximide. It was also found that cycloheximide exerted the inhibitory influence on the spontaneous culture-mediated expression of **CD23** on CD5+ but not CD5- B cells of the patients. However, the disappearance of **CD23** from CD5+ as well as CD5- B cells of cord blood samples was unaffected by the agent. These results strongly suggest that CD5+ B cells of RA patients may be specifically activated by some mechanisms responsible for the persistent expression of Fc epsilon RIIa mRNA leading to the accelerated turnover of **CD23** and in turn the increased release of sCD23.

L25 ANSWER 27 OF 31 MEDLINE

93346048 Document Number: 93346048. PubMed ID: 8344706. Variations in serum sCD23 in conditions with either enhanced humoral or cell-mediated immunity. Bansal A S; Ollier W; Marsh M N; Pumphrey R S; Wilson P B. (Regional Immunology Department, St Mary's Hospital, Manchester, U.K.) IMMUNOLOGY, (1993 Jun) 79 (2) 285-9. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Soluble **CD23** (sCD23) is increased by interleukin-4 (IL-4) and decreased by interferon-gamma (IFN-gamma). On the basis of cytokine

profiles T-helper (Th) cells may be functionally divided into IL-2- and IFN-gamma-secreting Th1 cells, which are involved in cell-mediated immunity (CMI), and IL-4- and IL-5-producing Th2 cells, which are involved in humoral immunity. Compared with sex-matched controls (median 8.5) we found significantly elevated levels of serum sCD23 in patients with rheumatoid **arthritis** (median 22.7, P < 0.0002), with the highest levels detected in patients fulfilling an increasing number of the American Association revised criteria for rheumatoid **arthritis**. Soluble **CD23** levels were also significantly raised in autoimmune thyroiditis (median 11.7, P < 0.02) and myasthenia gravis (median 10.4, P < 0.05). In contrast patients with either coeliac (median 6.5) or Crohn's disease (median 5.8) had reduced levels of sCD23 compared to appropriate controls (median 11.8), in both cases significant at P < 0.01. Variations in sCD23 may, therefore, reflect enhanced Th1 activity in the two later conditions in contrast to heightened Th2 activity within the three classical autoimmune conditions.

L25 ANSWER 28 OF 31 SCISEARCH COPYRIGHT 2003 ISI (R)
93:110185 The Genuine Article (R) Number: KM430. INCREASED PRODUCTION OF SOLUBLE **CD23** IN RHEUMATOID-**ARTHRITIS**, AND ITS REGULATION BY INTERLEUKIN-4. CHOMARAT P; BRIOLAY J; BANCHEREAU J; MIOSSEC P (Reprint). HOP EDOUARD HERRIOT, DEPT IMMUNOL, F-69374 LYON 08, FRANCE; HOP EDOUARD HERRIOT, DEPT RHEUMATOL, F-69374 LYON 08, FRANCE; SCHERING PLOUGH LAB IMMUNOL RES, DARDILLY, FRANCE; HOP EDOUARD HERRIOT, INSERM, U80, F-69374 LYON 08, FRANCE. ARTHRITIS AND RHEUMATISM (FEB 1993) Vol. 36, No. 2, pp. 234-242. ISSN: 0004-3591. Pub. country: FRANCE. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objective. To assess **CD23** status in rheumatoid **arthritis** (RA) patients, as defined by the levels of **CD23** expression on peripheral blood mononuclear cells (PBMC), the levels of soluble **CD23** (sCD23) in sera, and the production of sCD23 by PBMC cultures and its regulation by interleukin-4 (IL-4).

Methods. **CD23** expression as determined by double fluorescence-activated cell sorter analysis and sCD23 production as determined by immunoradiometric assay were investigated in 24 RA patients and 21 controls. Soluble **CD23** was measured in sera and supernatants of PBMC, activated with polyclonal activators (pokeweed mitogen [PWM] or Staphylococcus aureus Cowan strain 1, [SAC]) used either alone or in combination with IL-2 or IL-4.

Results. The percentage of B cells expressing **CD23** and serum levels of sCD23 were increased in patients with RA. IL-4 was a potent inducer of sCD23 production in supernatants, whereas IL-2 was inactive. Costimulation with SAC or PWM did not increase the effect obtained with IL-4 alone. When sCD23 levels in RA and control supernatants were compared, spontaneous production was found to be increased in RA PBMC. This difference from control values was even more pronounced when sCD23 levels in PBMC and purified B cells in response to IL-4, either alone or in combination with SAC or PWM, were tested. In the same supernatants, the increased secretion of sCD23 induced by IL-4 was associated with an inhibitory effect of IL-4 on Ig production, a phenomenon that was more pronounced in RA PBMC than in controls.

Conclusion. **CD23** status in RA is characterized by increased expression of **CD23** on B cells, increased production of sCD23 in sera and supernatants, and increased sensitivity of RA PBMC and B cells to IL-4.

L25 ANSWER 29 OF 31 MEDLINE
91231517 Document Number: 91231517. PubMed ID: 1827636.
Immunohistochemical demonstration of **CD23** expression on lymphocytes in rheumatoid synovitis. Hellen E A; Rowlands D C; Hansel T T; Kitas G D; Crocker J. (Department of Histopathology, East Birmingham Hospital.) JOURNAL OF CLINICAL PATHOLOGY, (1991 Apr) 44 (4) 293-6.

Journal code: 0376601. ISSN: 0021-9746. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The leucocyte antigen **CD23** is expressed by B lymphocytes following activation by a number of stimuli and functions as an IgE receptor, and in its soluble form, as a putative B cell growth factor. The expression of **CD23** on the surface of lymphocytes in paraffin wax sections of synovial biopsy specimens was studied using a novel mouse monoclonal **antibody**, BU38. Specimens were investigated from nine cases of rheumatoid **arthritis**, six cases of osteoarthritis, and eight cases of chronic inflammation in articular and non-articular tissues. **CD23** was expressed on a high proportion of lymphocytes in all forms of chronic inflammation and was not specific for rheumatoid **arthritis**. It may be a characteristic feature of any chronic inflammatory response. As **CD23** was found on the surface of lymphocytes in many cases of these arthritides, sCD23 in serum or synovial fluid may yet prove a useful marker for the severity of the inflammatory infiltrate.

L25 ANSWER 30 OF 31 MEDLINE

89289808 Document Number: 89289808. PubMed ID: 2472277. Expression and regulation of CD5 on in vitro activated human B cells. Freedman A S; Freeman G; Whitman J; Segil J; Daley J; Levine H; Nadler L M. (Division of Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA 02115.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1989 May) 19 (5) 849-55. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB The T cell-associated antigen CD5 has been shown to play an important role in the regulation of T cell activation. Monoclonal **antibodies** directed against CD5 upregulate helper function, and induce interleukin 2 (IL2) production by mature T cells as well as thymocytes. CD5 is also expressed on subsets of B cells associated with autoantibody production, and CD5+ B cells are present in increased numbers in patients with rheumatoid **arthritis** and systemic lupus erythematosis. More recently CD5 has been found to be present on human B lymphocytes following in vitro activation with phorbol myristate acetate. To date a similar functional role for CD5 has not to date been demonstrated for B cells. In this study we have shown that structurally similar CD5 molecules are present on activated B cells and T cells. In addition, CD5 on both stimulated B cells and T cells is phosphorylated, which may be important in the function of CD5 following activation. CD5 protein or mRNA was not detected on unstimulated splenic B cells depleted of any CD5+ cells. To investigate the control of CD5 expression, we examined a series of cytokines either alone or in combination for their effect on the induction of CD5. CD5 expression was specifically inhibited by IL4 but not by the other cytokines tested. This inhibition was very specific as IL4 did not inhibit the expression of other B cell activation antigens including CD25, B5, T9 and **CD23** as well as the pan-B cell antigen CD20. The addition of other cytokines did not increase or reverse the inhibition of CD5 expression by IL4. This inhibition was demonstrated by immunofluorescence and flow cytometric analysis. Immunoprecipitation studies of 125I-labeled activated B cells demonstrated that there was a decrease in cell surface CD5 protein, and not simply inhibition of expression of a particular epitope. Northern blot analysis demonstrated that the expression of CD5 mRNA was markedly inhibited in the presence of IL4, whereas the induction of the protooncogene c-myb was unaffected. This suggests that IL4 inhibits CD5 protein expression on activated B cells by reducing the amount of CD5 mRNA transcription or increasing the degradation of CD5 mRNA. The role of the T cell-derived lymphokine IL4 in regulating CD5 expression may be important in the disease states characterized by increased numbers of CD5+ B cells.

L25 ANSWER 31 OF 31 MEDLINE

90125215 Document Number: 90125215. PubMed ID: 2532990. Possible

different mechanisms of B cell activation in systemic lupus erythematosus and rheumatoid **arthritis**: opposite expression of low-affinity receptors for IgE (**CD23**) on their peripheral B cells. Kumagai S; Ishida H; Iwai K; Tsubata T; Umehara H; Ozaki S; Suginoshita T; Araya S; Imura H. (Second Division of Internal Medicine, Kyoto University Medical School, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1989 Dec) 78 (3) 348-53. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB To clarify the differential state of B cell activation in patients with systemic lupus erythematosus (SLE) and rheumatoid **arthritis** (RA), we investigated the expression of low-affinity receptor for IgE (Fc epsilon RII; **CD23**) on their peripheral B cells by a cytofluorometry using H107 (**CD23**) and Leu-16 (CD20) monoclonal **antibodies**. The percentage of **CD23**-negative B cells in total lymphocytes was significantly greater in both groups of patients than in normal subjects, suggesting the hyperactivity of late-phase B cells in both diseases. However, the increase of **CD23**-negative B cells in RA was brought about by the increased number of total B cells, although that in SLE was mainly based on the relative decrease of **CD23**-positive B cells. The number of IgD-positive B cells was decreased, and the number of colony-forming B cells was markedly increased in SLE patients. These observations indicate that a B cell abnormality is mainly qualitative in SLE but quantitative in RA.

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L27 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L27 ANSWER 2 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2001274349 EMBASE Low-grade non-Hodgkin's lymphoma in a patient with systemic **lupus erythematosus**. Robak T.; Robak E.; Bartkowiak J.; Blonski J.Z.; Niewiadomska H.; Wawrzyniak E.. Prof. T. Robak, Department of Hematology, Medical Univ. of Lodz, Copernicus Memorial Hospital, ul. Pabianicka 62, 93-513 Lodz, Poland. robaktad@psk2.am.lodz.pl. Leukemia and Lymphoma 41/5-6 (659-667) 2001.
Refs: 30.
ISSN: 1042-8194. CODEN: LELYEA. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Coexistence of systemic **lupus erythematosus** (SLE) with

low-grade non-Hodgkin's lymphoma (LGNHL) has been described occasionally in the literature with the potential pathogenetic role of monoclonal B CD5+/CD19+ cells. We report a case of LGNHL which developed 18 months after diagnosis of SLE. The monoclonal population of lymphocytes in the peripheral blood and bone marrow was CD5/CD19 negative but CD19/CD22 positive. The SLE responded well to treatment with prednisone and the course of the LGNHL was stable and cytotoxic treatment was not required.

L27 ANSWER 3 OF 25 MEDLINE
2000135837 Document Number: 20135837. PubMed ID: 10671190. Genetic dissection of B cell traits in New Zealand black mice. The expanded population of B cells expressing up-regulated costimulatory molecules shows linkage to Nba2. Wither J E; Paterson A D; Vukusic B. (Arthritis Centre of Excellence, The Toronto Hospital Research Institute, The Toronto Western Hospital, Toronto, Canada.. jwither@playfair.utoronto.ca) . EUROPEAN JOURNAL OF IMMUNOLOGY, (2000 Feb) 30 (2) 356-65. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB B cell abnormalities are a prominent feature of the immunologic derangement in NZB and NZB / W mice. We recently demonstrated that these mice have an increased proportion of splenic B cells expressing B7.1 and elevated levels of B7.2 and ICAM-1 that possess the characteristics of marginal zone B cells (**CD23**(low / -) CD5(-) CD44(hi) CD24(hi) IgD(- / low) IgM(hi)) and are found as early as 4 - 6 weeks of age. These findings suggest that activated B cells in NZB and NZB / W mice could serve a costimulatory function leading to activation of autoreactive T cells. However, it remains unclear whether there is any association between B abnormalities and nephritis in these mice. Here we have used genetic mapping techniques to address this issue. We show that increases in the proportion of B cells expressing costimulatory molecules, serum IgM levels, the number of IgM ELISpots, and IgG anti-single-stranded (ss) DNA **antibody** production, are significantly associated with a chromosomal region that overlaps with Nba2, a genetic locus previously linked to nephritis. Based on these findings we propose that immune mechanisms leading to polyclonal B cell activation and up-regulation of costimulatory molecules in these mice play a central role in the loss of tolerance that leads to production of pathogenic autoantibodies.

L27 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L27 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS
1999:736800 Document No. 132:48911 Induction of autoimmunity in a transgenic model of B cell receptor peripheral tolerance: changes in coreceptors and

B cell receptor-induced tyrosine-phosphoproteins. Feuerstein, Nili; Chen, Fangqi; Madaio, Michael; Maldonado, Michael; Eisenberg, Robert A. (Division of Rheumatology, Department of Medicine, University of Pennsylvania, Philadelphia, PA, 19104, USA). Journal of Immunology, 163(10), 5287-5297 (English) 1999. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB Abrogation of peripheral tolerance in transgenic mice that express a uniform B-cell receptor may create a powerful tool to examine the mol. mechanisms that underlie the autoimmune response in B cells. Here the authors report that processes that induce a systemic **lupus erythematosus**-like syndrome in normal mice, namely chronic graft vs. host reaction, trigger systemic autoimmunity in a well-established transgenic mice model of B cell receptor peripheral tolerance. The induction of graft vs. host reaction in mice that carry both a rearranged B cell Ag receptors specific for hen egg lysozyme and expressing chronically circulating hen egg lysozyme Ag resulted in induction of high and sustained levels of circulating anti-hen egg lysozyme autoantibodies and glomerulonephritis with proteinuria. This was assocd. with marked changes in expression of cell-surface proteins, such as **CD23** and complement receptor 2. B cells from the graft vs. host-induced mice could proliferate in vitro in response to self-Ag, and upon stimulation with anti-IgD demonstrated rapid phosphotyrosine phosphorylation of specific proteins, which could not be induced in the anergic double transgenic B cells. Conversely, loss of tolerance was not assocd. with a higher induction in the level of Syk kinase phosphorylation following stimulation with anti-IgD. Taken collectively, these data establish that (1) processes that induce a systemic **lupus erythematosus** -like syndrome in normal mice can abrogate peripheral tolerance in transgenic mice expressing self-tolerized B cells, and that (2) loss of tolerance in this model is assocd. with marked changes in surface expression of B cell coreceptors as well as with selective changes in IgD-induced signaling by discrete tyrosine-phosphoproteins, but not Syk kinase.

L27 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS

2000:19944 Document No. 132:278079 Study on the function of sCD23 in SLE. Zhang, Kaiming; Yin, Xingping; Zhou, Ming; Chang, Wenjuan; Guo, Zhijie (Department of Dermatology, Taiyuan Central Hospital, Taiyuan, 030009, Peop. Rep. China). Zhonghua Weishengwuxue He Mianyixue Zazhi, 19(3), 250-252 (Chinese) 1999. CODEN: ZWMZDP. ISSN: 0254-5101. Publisher: Weishenbu Beijing Shengwu Zhipin Yanjiuso.

AB The levels of sCD23 in sera and the expression of **CD23** in cutaneous lesions and peripheral blood mononuclear cells (PBMC) from SLE patients were evaluated with ELISA and immunohistochem. techniques, resp., then the relationship of **CD23** system with the titers of ANA, anti-dsDNA-IgG, was studied. The levels of sCD23 in patients were significantly higher than controls. Furthermore, in comparison to the static stage, the sCD23 of patients with active disease was markedly higher. The correlation between **CD23** and ANA, anti-dsDNA-IgG was stronglyl pos. The expression of **CD23** was weak only in minor lesions (3/9 but strong on the PBMC from all patients. The **CD23** system may play a key role in SLE, mainly the antigen presentation process, further promoting the differentiation and proliferation of B lymphocytes and prodn. of autoantibodies. **CD23** may also be an indicator for monitoring the activity of SLE.

L27 ANSWER 7 OF 25 MEDLINE

1998359324 Document Number: 98359324. PubMed ID: 9696135. Defective early T and T-dependent B cell activation in systemic **lupus erythematosus**. Fernandez-Gutierrez B; de Miguel S; Morado C; Hernandez-Garcia C; Banares A; Jover J A. (Rheumatology Service, Hospital Clinico San Carlos, Madrid, Spain.) LUPUS, (1998) 7 (5) 314-22. Journal code: 9204265. ISSN: 0961-2033. Pub. country: ENGLAND: United Kingdom.

Language: English.

AB Systemic **lupus erythematosus** (SLE) is characterized by autoantibody production of unknown origin. Since T-B cell interaction is a key event to produce **antibodies**, we investigated this interaction through study of CD69, CD40 ligand (CD40L) and **CD23** expression (three very early activation antigens). Peripheral blood mononuclear cells (PBMC) from inactive lupus patients were studied following culture with either medium alone, anti-CD3 monoclonal **antibody** (mAb), recombinant interleukin-4 (rIL-4) or phorbol myristate acetate (PMA)+/-ionomycin. Analysis of **CD23** expression on lupus B cells in basal conditions and after anti-CD3 challenge of PBMC, a reflection of cognate interaction between T and B cells, was clearly defective. Conversely, **CD23** expression on lupus B cells following non-cognate T cell signals (rIL-4) was preserved. CD69 and CD40L expression was also impaired in lupus T cells following anti-CD3 challenge. Nonetheless, activation by means of PMA and/or ionomycin was preserved both in T cells (CD69 and CD40L expression) and in B cells (**CD23** expression). These results indicate that B cells from inactive lupus patients display a normal early response to direct B-cell stimuli. Conversely, T-dependent B-cell stimuli are clearly defective in SLE patients in remission. These results indicate that T-B cognate interaction related to defective T cell activation located between surface membrane and protein kinase C (PKC)/ionomycin function is an intrinsic characteristic of these patients.

L27 ANSWER 8 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

97363262 EMBASE Document No.: 1997363262. Systemic **lupus erythematosus** complicated by disseminated intravascular coagulation: The role of serum soluble cell surface markers. Kogure T.; Fujinaga H.; Nozaki K.; Sakai S.; Itoh T.; Terasawa K.. Dr. T. Kogure, Dept. af Japanese Oriental Med., Faculty of Medicine, Toyanza Med./Pharmaceutical Univ., 2630 Sugitani, Toyama 930-01, Japan. Clinical and Experimental Rheumatology 15/6 (671-675) 1997.
Refs: 24.
ISSN: 0392-856X. CODEN: CERHDP. Pub. Country: Italy. Language: English. Summary Language: English.

AB We describe a 31-year-old Japanese female patient with systemic **lupus erythematosus** (SLE), who developed disseminated intravascular coagulation (DIC), fever, erythema on the hands, and aphthous stomatitis despite the absence of circulating anticoagulant. Since no other cause for DIC besides SLE could be demonstrated, she was treated with prednisolone and anticoagulants, which rapidly corrected the DIC as well as the other manifestations of SLE. During the episode of DIC, elevated serum anti-DNA **antibody** titers and decreased serum complement concentrations were not observed. In contrast, the serum concentration of soluble CD8 (sCD8) paralleled SLE disease activity. In addition, the concentration of plasma thrombomodulin was also increased. These observations suggest that the serum concentration of sCD8 is related to the clinical aspects of SLE, and that vasculitis might contribute to the development of SLE-associated DIC.

L27 ANSWER 9 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

97:485742 The Genuine Article (R) Number: XF564. Genetic dissection of systemic **lupus erythematosus** pathogenesis - Sle2 on murine chromosome 4 leads to B cell hyperactivity. Mohan C; Morel L; Yang P; Wakeland E K (Reprint). UNIV FLORIDA, DEPT PATHOL IMMUNOL & LAB MED, BOX 100275, GAINESVILLE, FL 32610 (Reprint); UNIV FLORIDA, DEPT PATHOL IMMUNOL & LAB MED, GAINESVILLE, FL 32610; UNIV FLORIDA, CTR MAMMALIAN GENET, GAINESVILLE, FL 32610. JOURNAL OF IMMUNOLOGY (1 JUL 1997) Vol. 159, No. 1, pp. 454-465. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Susceptibility to systemic **lupus erythematosus** in the NZM2410 murine model maps to Sle1, Sle2, Sle3, and the H2 loci, To unravel how these loci contribute to the pathogenesis of lupus, individual NZM2410-derived genomic intervals bearing these loci have been successfully backcrossed onto the resistant C57BL/6 (B6) background, The focus of this study was to understand how Sle2 OH murine chromosome 4 impacts the immune system, Compared with C57BL/6 (B6) mice, B6 mice congenic for Sle2 exhibit: a variety of immunophenotypes affecting their B cells, They have an early, but transient, expansion of splenic, **CD23**(low) B cells, Thereafter, their B cells appear activated by surface phenotype and functional criteria, paralleled by elevated serum levels of polyreactive/polyclonal IgM. Importantly, Sle2 leads to a heightened B cell responsiveness to in vitro stimuli and to in vivo antigenic challenge. Finally, they exhibit increased levels of peritoneal and splenic B1 cells, Thus, Sle2 harbors a gene that leads to B cell hyperactivity and elevated B1 cell formation. However, Sle2 by itself on the normal B6 background is insufficient to generate IgG antinuclear Abs (ANA) or nephritis. By reducing the B cell signaling threshold, Sle2 might serve to amplify an ongoing autoimmune response.

L27 ANSWER 10 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1998:6398 Document No.: PREV199800006398. Study of expression of **CD23** on peripheral blood mononuclear cells in patients systemic **lupus erythematosus**. Li, Xiqing; Ling, Shaoxian; Wang, Bin. Dep. Dermatol., Sun Yat-Sen Meml. Hosp., Sun Yat-Sen Univ. Med. Sci., Guangzhou 510120 China. Zhonghua Pifuke Zazhi, (Oct., 1997) Vol. 30, No. 5, pp. 324-326. ISSN: 0412-4030. Language: Chinese. Summary Language: Chinese; English.

AB In order to study the relationship between expression of **CD23** on B cells and the development of SLE, and possible role in the pathogenesis of SLE, we used ABC immunohistochemistry and Northern dot-blot hybridization technique to detect **CD23** protein and mRNA expression on PBMC in SLE patients and healthy controls. The results showed: **CD23** protein and mRNA expression was significantly higher in active SLE patients than those in controls ($P<0.01$), and showed positive linear correlation between **CD23** expression and disease activity ($rs = 0.3814, P<0.05$), but there was no significant difference between the patients after treatment in comparison with controls ($P>0.05$). There were no significant difference ($P>0.05$) in the expression of **CD23** protein on PBMC among active SLE patients with different levels of ANA or dsDNA **antibody**, with or without renal or brain involvement as well as treated with corticosteroids and/or other immunosuppressants. It was implicated that abnormal activation and proliferation of B cells lead to over expression of **CD23** protein and mRNA in active SLE, but there was not direct relationship between over expression of **CD23** and the levels of ANA or anti-dsDNA **antibody**.

L27 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS
1997:353668 Document No. 127:16300 Clinical significance of soluble CD4, CD8, **CD23** molecules in rheumatic diseases. Sawada, Shigemasa (Sch. Med., Nihon Univ., Tokyo, 179, Japan). Nichidai Igaku Zasshi, 56(3), 114-116 (Japanese) 1997. CODEN: NICHAS. ISSN: 0029-0424. Publisher: Nihon Daigaku Igakkai.

AB A review with 16 refs. Changes in the serum levels of sol. forms of CD4, CD8 and **CD23** (sCD4, sCD8, sCD23) are reported in human autoimmune diseases. SCD4 level increases and sCD8 level decreases in primary Sjoegren's syndrome, and the levels are comparable to normal subjects in secondary Sjoegren's syndrome. Serum IgG level strongly correlates with sCD4 level. SCD4 and sCD8 levels increase in systemic **lupus erythematosus** (SLE). SCD4 level correlates with serum IgG level, esp. with anti-DNA **antibody** level and not with the other autoimmune **antibody** levels as anti-ribonucleoprotein

(RNP) **antibody**. SCD4 level correlates with serum complement level, and sCD8 correlates with erythrocyte sedimentation rate (ESR). SCD4, sCD8 and sCD23 levels increase in rheumatoid arthritis (RA). SCD8 level correlates with ESR and C-reactive protein (CRP) level. sCD23 level correlates with ESR, CRP and rheumatoid factor level. abs; sCD8 level increases in acute virus infection, and chronic elevation of sCD4 level suggests human immunodeficiency virus (HIV) infection or HIV-related retrovirus infection.

L27 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L27 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L27 ANSWER 14 OF 25 MEDLINE
97131831 Document Number: 97131831. PubMed ID: 8977305. CD40-mediated stimulation of B1 and B2 cells: implication in autoantibody production in murine lupus. Kaneko Y; Hirose S; Abe M; Yagita H; Okumura K; Shirai T. (Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Dec) 26 (12) 3061-5. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany,

Federal Republic of. Language: English.

AB B1 cells usually show preferential responses to T cell-independent antigens. To ask whether B1 cells could respond to CD40-mediated stimulation for proliferation and differentiation, and whether CD40-mediated signals are involved in the production of autoantibodies by B1 cells, we compared responses to our newly established agonistic anti-mouse CD40 monoclonal **antibody** (mAb) between B1 and B2 cells from autoimmune-prone (NZB x NZW) F1 mice. Stimulation with this mAb induced a similar level of proliferative responses of both B1 and B2 cells, as well as an increase in expression of cell surface molecules I-A, CD54, **CD23**, CD80, and CD86. While co-stimulation with interleukin (IL)-4 markedly augmented proliferative as well as IgG1 and IgE **antibody** responses of both B and B2 cells, co-stimulation with IL-5 augmented proliferative and IgM **antibody** responses of only B1 cells. Splenic B1, but not B2 cells from young (NZB x NZW) F1 mice spontaneously produced substantial amounts of IgM including IgM anti-DNA **antibodies**, and the levels increased in case of stimulation with anti-CD40 mAb alone, or to a greater extent with the mAb plus IL-4 and IL-5. Collectively, these results indicate that splenic B1 cells from autoimmune (NZB x NZW) F1 mice have a comparable responsiveness to the CD40-mediated stimulation to that of B2 cells, which would be a potent regulatory mechanism involved in the spontaneous production of autoantibodies by B1 cells.

L27 ANSWER 15 OF 25 MEDLINE

96292514 Document Number: 96292514. PubMed ID: 8743127. In vitro type-1 and type-2 cytokine production in systemic **lupus erythematosus**: lack of relationship with clinical disease activity. Barcellini W; Rizzardi G P; Borghi M O; Nicoletti F; Fain C; Del Papa N; Meroni P L. (Institute of Internal Medicine, Immunopathology and Infectious Diseases, University of Milan, Italy.) LUPUS, (1996 Apr) 5 (2) 139-45. Journal code: 9204265. ISSN: 0961-2033. Pub. country: ENGLAND: United Kingdom. Language: English.

AB OBJECTIVE: To investigate the relationship between disease activity and in vitro cytokine, soluble(s)**CD23** and polyclonal and anti-DNA **antibody** production by PBMC from patients with active systemic **lupus erythematosus** (SLE). METHODS: Cytokines, sCD23 and immunoglobulins were estimated by ELISA in unstimulated and polyclonal mitogen-stimulated culture supernatants. RESULTS: PHA-induced IL-2 and IFN-gamma production were decreased, whereas spontaneous and PHA-induced IL-6 and IL-10 production were increased in cultures of SLE lymphocytes. Conversely, spontaneous and PHA-stimulated IL-4 and sCD23 production was comparable between patients and controls. Finally, we found an increase in in vitro spontaneous polyclonal and anti-DNA IgG secretion. CONCLUSIONS: We demonstrated an expanded type-2 cytokine profile with no correlation with parameters of disease activity.

L27 ANSWER 16 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

96:759060 The Genuine Article (R) Number: VL947. ELEVATED LEVELS OF SOLUBLE FC-EPSILON-RII/**CD23** AND **ANTIBODIES** TO EPSTEIN-BARR-VIRUS IN PATIENTS WITH SJOGRENS-SYNDROME. SUZUKI M (Reprint); NAGATA S; HIRAMATSU K; TAKAGI I; ITO H; KITAO S; ITO M; OHTA N; BABA S. NAGOYA CITY UNIV, SCH MED, DEPT OTORHINOLARYNGOL, MIZUHO KU, 1 KAWASUMI, NAGOYA, AICHI 467, JAPAN (Reprint); NAGOYA CITY UNIV, SCH MED, DEPT MED ZOOL, NAGOYA, AICHI 467, JAPAN. ACTA OTO-LARYNGOLOGICA (1996) Supp. 525, pp. 108-112. ISSN: 0001-6489. Pub. country: JAPAN. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To clarify how Epstein-Barr virus (EBV) infection is responsible for Sjogren's syndrome (SjS) we measured both IgG and IgM **antibodies** to viral capsid antigen (VCA) of EBV in the sera of normal healthy subjects and patients with SjS. Anti-VCA IgG was detectable in all controls and patients; however, anti-VCA IgG titers in the sera of SjS

patients were significantly higher than those of the controls ($p < 0.01$). No anti-VCA IgM was detected in the sera of controls whereas anti-VCA IgM was detected in the sera from 10 out of the 13 patients with SjS. This suggests that SjS might be associated with EBV. The serum levels of sCD23 (IgE-binding factor) were also measured to assess the differential state in patients with SjS. The sCD23 level of normal individuals was 211.26+/-12.01 mu g/L (value is mean+/-SE), and was 443.77+/-71.94 mu g/L in the 13 patients with SjS The mean sCD23 level in the 9 patients with SjS without any complication was 360.67+/-35.63 mu g/L. In the patients with SjS, sCD23 levels were significantly higher than those in the normal individuals ($p < 0.01$).

L27 ANSWER 17 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)
96:43242 The Genuine Article (R) Number: TL347. INCREASED SOLUBLE **CD23** MOLECULES IN SERUM/SALIVA AND CORRELATION WITH THE STAGE OF SIALOECTASIS IN PATIENTS WITH PRIMARY SJOGRENS-SYNDROME. TAKEI M; AZUHATA T; YOSHIMATU T; SHIGIHARA S; HASHIMOTO S; HORIE T; HORIKOSHI A; SAWADA S (Reprint). NIHON UNIV, HERIMA HIKARIGAOKA HOSP, SCH MED, DEPT INTERNAL MED, NERIMA KU, 2-11-1 HIKARIGAOKA, TOKYO 179, JAPAN (Reprint); NIHON UNIV, HERIMA HIKARIGAOKA HOSP, SCH MED, DEPT INTERNAL MED, NERIMA KU, TOKYO 179, JAPAN; NIHON UNIV, ITABASHI HOSP, SCH MED, DEPT INTERNAL MED 1, TOKYO, JAPAN; NIHON UNIV, NERIMA HIKARIGAOKA HOSP, DEPT OTOLARYNGOL, TOKYO, JAPAN. CLINICAL AND EXPERIMENTAL RHEUMATOLOGY (NOV/DEC 1995) Vol. 13, No. 6, pp. 711-715. ISSN: 0392-856X. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Objective. We examined the soluble **CD23** (sCD23) molecules in sera and saliva from patients with Sjogren's syndrome.
Methods. The determination of sCD23 and other soluble molecules were made by the enzyme-linked immunosorbent assay.
Results. The amounts of sCD23 in the sera/saliva were significantly increased in the patients compared to the controls and the levels were significantly correlated with sialoectasis.
Conclusion. The findings suggest that increased sCD23 molecules in saliva from patients with Sjogren's syndrome may reflect active sialoectasis.

L27 ANSWER 18 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
94084024 EMBASE Document No.: 1994084024. Soluble Fc.epsilon.RII/**CD23** in patients with autoimmune diseases and Epstein-Barr virus-related disorders: Analysis by ELISA for soluble Fc.epsilon.RII/**CD23**.
Yoshikawa T.; Nanba T.; Kato H.; Hori K.; Inamoto T.; Kumagai S.; Yodoi J.. Department of Biological Responses, Institute for Virus Research, Kyoto University, 53 Shogoin-Kawahara-cho,Sakyo, Kyoto 606-01, Japan.
ImmunoMethods 4/1 (65-71) 1994.
ISSN: 1058-6687. CODEN: IMUME8. Pub. Country: United States. Language: English. Summary Language: English.
AB The low-affinity Fc receptor for IgE (Fc.epsilon.RII/**CD23**) and its soluble form (sCD23, IgE-binding factor) have multiple functions, and enhanced levels of these are associated with various immunological diseases. We established two sensitive ELISA systems using enzyme-conjugated mAb and biotinylated mAb. The detection limits of the ELISA systems were 0.03 and 1.0 ng/ml, which showed good correlation in the range 1.0-10 ng/ml. In the ELISA system using enzyme-conjugated mAb, the average sCD23 concentration in 303 normal healthy volunteers was 1.4 .+-. 0.3 ng/ml. In the ELISA system using biotinylated mAb, sCD23 levels in normal healthy volunteers showed almost the same values. In patients with autoimmune diseases such as rheumatoid arthritis, systemic **lupus erythematosus**, Sjogren syndrome, progressive systemic sclerosis, and mixed connective tissue disease, the sCD23 levels were significantly higher than those in normal individuals. Furthermore, in Epstein-Barr virus-related disorders after liver transplantation with immunosuppression, plasma levels of sCD23 rapidly increased to more than

12 ng/ml when clinical symptoms were evident. In addition, the sCD23 values remained high, although elevated GOT levels gradually decreased to standard values and EBV hepatitis improved. These data suggest that sCD23 levels are a sensitive marker of autoimmune diseases and EBV-related disorders in addition to allergic disorders. The ELISA system for sCD23 may be an additional diagnostic tool in estimating the clinical courses of these diseases.

L27 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2003 ACS
1993:493523 Document No. 119:93523 Murine and human cytokine (CD40-L) which binds to CD40, and soluble CD40 and CD40 fusion molecules. Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K. (Immunex Corp., USA). PCT Int. Appl. WO 9308207 A1 19930429, 79 pp. DESIGNATED STATES: W: AU, CA, FI, JP, KR, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US8990 19921023. PRIORITY: US 1991-783707 19911025; US 1991-805723 19911205.
AB The title CD40-L mols. are disclosed, as are related DNA sequences, vectors, and transformed host cells. The murine and human CD40-L polypeptides bind to the extracellular binding region of a CD40 receptor. Also provided are a CD40/IgG1 Fc region fusion protein and a sol. CD40 protein (sCD40) comprising the extracellular portion of CD40; both the CD40/Fc and sCD40 can inhibit CD40-L or anti-CD40 monoclonal **antibody**-induced B-cell stimulation, interleukin-4-induced IgE stimulation, and interleukin-4-induced **CD23** induction in B-cells. Construction is described of a CD40/Fc DNA for prodn. of a fusion protein for use in detecting cDNA clones encoding a CD40 ligand. Also described are selection of a cell line putatively expressing CD40-L, prepn. of a cDNA library for expression cloning of murine CD40-L, cross-species hybridization methodol. used to isolate a human CD40-L homolog, anti-allergy therapeutic effects of sCD40 and CD40/Fc fusion protein, etc. Interaction of CD40 with its ligand was evidently the principal mol. interaction responsible for T-cell contact-dependent induction of B-cell growth and differentiation to both antigen-specific **antibody** prodn. and polyclonal Ig secretion.

L27 ANSWER 20 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)
91:141712 The Genuine Article (R) Number: FA425. EVIDENCE FOR DIFFERENTIAL RESPONSIVENESS OF HUMAN CD5+ AND CD5- B-CELL SUBSETS TO T CELL-INDEPENDENT MITOGENS. ZUPO S (Reprint); DONO M; AZZONI L; CHIORAZZI N; FERRARINI M. IST SCI STUDIO & CURA TUMORI, IST NAZL RIC CANC, SERV IMMUNOL CLIN, VIALE BENEDETTO XV 10, I-16132 GENOA, ITALY (Reprint); UNIV TURIN, DIPARTIMENTO SCI BIOMED & ONCOL UMANA, I-10124 TURIN, ITALY; CORNELL UNIV, N SHORE UNIV HOSP, COLL MED, DEPT MED, MANHASSET, NY, 11030. EUROPEAN JOURNAL OF IMMUNOLOGY (1991) Vol. 21, No. 2, pp. 351-359. Pub. country: ITALY; USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Tonsillar resting B cells were separated into CD5+ and CD5- cell subsets and stimulated with the thymus-independent mitogens, Staphylococus aureus Cowan strain I (SAC) or insolubilized anti-mu monoclonal **antibodies** (a-mu-Ab). CD5+ cells incorporated [H-3]thymidine more efficiently than unfractionated cells when stimulated with SAC and their response was augmented by the addition of interleukin (IL)2 to the cultures. CD5+ cells also proliferated in response to a-mu-Ab provided that IL 2 was present. SAC-, but not a-mu-Ab-stimulated CD5+ cells produced IgM and IgG molecules when IL 2 was added to th cultures and also secreted autoantibodies with rheumatoid factor activity and sometimes also with anti-single-stranded, but not double-stranded, DNA activity. The efficient response of CD5+ cells was not explained by the fact that they contained cells already activated in vivo. Thus, they did not express the **CD23**, CD69, CD71 and CD39 activation markers, failed to incorporated [H-3]thymidine and to secrete Ig spontaneously or in response to IL 2 and were found to be in a quiescent state by cell cycle flow cytometric analysis.

In contrast to CD5+ cells, CD5- cells displayed very little or no [H-3]thymidine incorporation in response to SAC or to a-mu-Ab and their poor responsiveness was not altered by changing either the doses of the stimulants, the timing of the cultures, by co-culturing the cells together with CD5+ cells, or by adding IL 2 or IL 4. Immunofluorescence studies showed that freshly prepared CD5- cells did not have surface activation markers but that they expressed them following SAC stimulation. Thus, unlike that observed for CD5+ cells, SAC seems to be capable of activating CD5- cells but does not appear to be a sufficient stimulus for driving the cells into the subsequent phases of the cell cycle.

The above findings, that demonstrate marked differences in the response to CD5+ and CD5- cells to thymus-independent stimuli, may bear relevance for the understanding of the normal clonal expansion of CD5+ cells as well as for the pathogenesis of autoimmune diseases.

L27 ANSWER 21 OF 25 MEDLINE

91166592 Document Number: 91166592. PubMed ID: 1825912. In vitro regulation of B cell differentiation by interleukin-6 and soluble **CD23** in systemic **lupus erythematosus** B cell subpopulations and antigen-induced normal B cells. Klashman D J; Martin R A; Martinez-Maza O; Stevens R H. (Department of Medicine, University of California, Los Angeles School of Medicine 90024.) ARTHRITIS AND RHEUMATISM, (1991 Mar) 34 (3) 276-86. Journal code: 0370605. ISSN: 0004-3591. Pub. country: United States. Language: English.

AB Polyreactive systemic **lupus erythematosus** (SLE) B cells were compared with antigen-induced SLE and normal B cells for their interleukin-6 (IL-6) and soluble **CD23** requirements. Unlike normal B cells, secretion of **antibody** by SLE B cells in serum-free medium was not enhanced by exogenous IL-6. Anti-IL-6 **antibodies** inhibited immunoglobulin production in cultures of normal and SLE B cells, which suggests that IL-6 is required for B cell differentiation. SLE culture supernatants had elevated levels of IL-6, which explains the poor response of the SLE cells to exogenous IL-6. Soluble **CD23** enhanced the responses of cells from normal subjects and SLE patients.

L27 ANSWER 22 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

91087722 EMBASE Document No.: 1991087722. Cytokine-independent progression of immunoglobulin production in vitro by B lymphocytes from patients with systemic **lupus erythematosus**. Pelton B.K.; Speckmaier M.; Hylton W.; Farrant J.; Denman A.M.. Div. Immunological Medicine, Clinical Research Centre, Northwick Park Hospital, Watford Road,Harrow, Middlesex HA1 3UJ, United Kingdom. Clinical and Experimental Immunology 83/2 (274-279) 1991.
ISSN: 0009-9104. CODEN: CEXIAL. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB B lymphocytes from patients with systemic **lupus erythematosus** (SLE) secreted high levels of immunoglobulin spontaneously when cultured in vitro. Addition of the cytokines interleukin-2, interleukin-4 and interleukin-6 either alone or in combination failed to augment spontaneous immunoglobulin synthesis. Percoll-separated low-density SLE B lymphocytes matured into immunoglobulin-secreting cells also independent of exogenous interleukins. During maturation these cells became enlarged and less dense, and began to express **CD23**. This was in contrast to normal B cells, which did not secrete immunoglobulin spontaneously but synthesized IgM after interleukin stimulation. These results indicate that in vitro immunoglobulin synthesis by SLE B cells is already initiated in these cells and progresses independently of further stimulatory manoeuvres.

L27 ANSWER 23 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

91:302666 The Genuine Article (R) Number: FL932. PROLIFERATIVE RESPONSES OF B-CELLS FROM ELDERLY HUMANS - ABNORMALITIES IN EARLY RESPONSIVENESS ARE

RELATED TO ALTERATIONS IN B-CELL ACTIVATION MOLECULES. WHISLER R L (Reprint); NEWHOUSE Y G; CHEN J R. OHIO STATE UNIV, WILLIAM H DAVIS MED RES CTR, DEPT INTERNAL MED, 480 W 9TH AVE, COLUMBUS, OH, 43210 (Reprint). LYMPHOKINE AND CYTOKINE RESEARCH (1991) Vol. 10, No. 1-2, pp. 1-6. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Age-related changes are known to occur in the function of human T cells but less information is available about human B cells during aging. In this study, B cells obtained by negative selection from the peripheral blood of young and elderly subjects were stimulated in vitro with anti-IgM, Staphylococcus aureus Cowan strain I (SAC), or Staph protein A (SpA) from SAC. Their proliferative capabilities with and without lymphokines were quantitated by [H-3]thymidine uptake. Stimulated B cells from elderly subjects were reduced in their overall ability to sustain normal levels of proliferation observed for B cells from young subjects. However, time course studies analyzing early proliferative responses revealed that B cells from one subset of elderly displayed persistent hyporesponsiveness whereas another subset demonstrated early hyperresponsiveness compared to B cells from young adults. Experiments to determine the frequencies of B cells with transferrin receptors (TfR) and low-affinity receptors for IgE (Fc-epsilon-RII/**CD23**) showed reductions in the expression of these two glycoproteins among stimulated B cells from elderly with the persistent decreases in proliferation. By contrast, unstimulated B cells of elderly subjects with early hyperresponsiveness displayed increased frequencies of TfR-positive cells, which became reduced after stimulation. Further, stimulated B cells from this group demonstrated greater frequencies of **CD23** positive cells than young adults (13 vs. 8%). Thus two distinct profiles of proliferative abnormalities can be observed in early cohorts of activated B cells from elderly humans. The association of these abnormalities with differences in TfR and **CD23** suggests that certain age-related defects occur relatively early during the B cell activation scheme.

L27 ANSWER 24 OF 25 MEDLINE

90125215 Document Number: 90125215. PubMed ID: 2532990. Possible different mechanisms of B cell activation in systemic **lupus erythematosus** and rheumatoid arthritis: opposite expression of low-affinity receptors for IgE (**CD23**) on their peripheral B cells. Kumagai S; Ishida H; Iwai K; Tsubata T; Umehara H; Ozaki S; Suginoshita T; Araya S; Imura H. (Second Division of Internal Medicine, Kyoto University Medical School, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1989 Dec) 78 (3) 348-53. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB To clarify the differential state of B cell activation in patients with systemic **lupus erythematosus** (SLE) and rheumatoid arthritis (RA), we investigated the expression of low-affinity receptor for IgE (Fc epsilon RII; **CD23**) on their peripheral B cells by a cytofluorometry using H107 (**CD23**) and Leu-16 (CD20) monoclonal **antibodies**. The percentage of **CD23**-negative B cells in total lymphocytes was significantly greater in both groups of patients than in normal subjects, suggesting the hyperactivity of late-phase B cells in both diseases. However, the increase of **CD23**-negative B cells in RA was brought about by the increased number of total B cells, although that in SLE was mainly based on the relative decrease of **CD23**-positive B cells. The number of IgD-positive B cells was decreased, and the number of colony-forming B cells was markedly increased in SLE patients. These observations indicate that a B cell abnormality is mainly qualitative in SLE but quantitative in RA.

L27 ANSWER 25 OF 25 MEDLINE

89009850 Document Number: 89009850. PubMed ID: 3262675. Production of B cell-stimulating factors by B cells in patients with systemic **lupus erythematosus**. Tanaka Y; Saito K; Shirakawa F; Ota

T; Suzuki H; Eto S; Yamashita U. (First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan.) JOURNAL OF IMMUNOLOGY, (1988 Nov 1) 141 (9) 3043-9. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The production of B cell-stimulating factors (BSF) by B cells in patients with systemic **lupus erythematosus** (SLE) was studied in vitro. B cells from SLE patients markedly proliferated and differentiated into Ig-producing cells by in vitro culture without any stimulation. The culture supernatant of these B cells contained BSF activity that stimulated Staphylococcus aureus Cowan I-treated normal B cells to proliferate and differentiate into Ig-producing cells. By a Percoll gradient density centrifugation, BSF-producing cells were enriched in the higher density fraction, but were reduced in the lower density fraction. The BSF also stimulated the proliferation and the differentiation of SLE B cells. By a Percoll gradient density centrifugation, SLE B cells responsive to the BSF were enriched in the higher density fraction, but were reduced in the lower density fraction. The Mr of the BSF was estimated as about 18,000 Da by Sephacryl S-200 column chromatography. The BSF fraction did not possess IL-2 and IFN activity, but possessed IL-1 activity, which stimulated murine thymocyte proliferative responses. The BSF activity was partially, but not completely, absorbed by an anti-IL-1 alpha **antibody**. Furthermore, the BSF possessed IL-4 activity, which induced not only the proliferative responses of normal B cells stimulated with B cell mitogens, but also the expression of low affinity Fc epsilon R/**CD23** on normal B cells. The BSF also possessed IL-6 activity, which induced the proliferative responses of IL-6-dependent hybridoma cells, MH-60 BSF2. Moreover, human rIL-1, rIL-4, and rIL-6 stimulated SLE B cells. These results suggest that SLE B cells spontaneously produce the BSF such as IL-1 alpha, IL-4, and IL-6 and express their receptors on their surface, and the interaction between the BSF and their receptors stimulates SLE B cells to spontaneously proliferate and differentiate into Ig-producing cells as an autocrine mechanism.

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L28         192 L23 AND TREATMENT

=> s l28 and arthritis
L29           8 L28 AND ARTHRITIS

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L30 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS

2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in

combination, and in either, over prolonged periods of time.

L30 ANSWER 2 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2001299562 EMBASE Lymphoma in a patient with rheumatoid **arthritis** receiving methotrexate **treatment**: Successful **treatment** with rituximab. Stewart M.; Malkovska V.; Krishnan J.; Lessin L.; Barth W.. Dr. W. Barth, 2021 K Street, NW, Washington, DC 20006, United States. wfbarth@worldnet.att.net. Annals of the Rheumatic Diseases 60/9 (892-893) 2001.
Refs: 18.
ISSN: 0003-4967. CODEN: ARDIAO. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB A 55 year old man with chronic lymphocytic leukaemia (CLL) and rheumatoid **arthritis** (RA), treated for four years with methotrexate (MTX), who developed a B cell non-Hodgkin's lymphoma (B-NHL), is described. The tumour was localised to the shoulder and axillary lymph nodes, and positive for Epstein-Barr viral antigens. After failure of radiation and chemotherapy, a complete remission was achieved with a combination of **antibody treatment** (rituximab) and EPOCH. The development of a second malignancy in a patient with RA receiving MTX has not been described before. The summation of T cell deficiencies induced by MTX, CLL, and RA may all have contributed to the development of the B-NHL.

L30 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L30 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to **CD23** useful in the **treatment** of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative **treatment** of mice against **arthritis** using

monoclonal anti-**CD23 antibody, CD23**
-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L30 ANSWER 5 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
96303695 EMBASE Document No.: 1996303695. The presence of interleukin-13 in rheumatoid synovium and its antiinflammatory effects on synovial fluid macrophages from patients with rheumatoid **arthritis**. Isomaki P.; Luukkainen R.; Toivanen P.; Punnonen J.. Department of Medical Microbiology, Turku University, Kiinamyllynkatu 13,FIN-20520 Turku, Finland. Arthritis and Rheumatism 39/10 (1693-1702) 1996. ISSN: 0004-3591. CODEN: ARHEAW. Pub. Country: United States. Language: English. Summary Language: English.

AB Objective. To study the production of interleukin-13 (IL-13) in rheumatoid synovium and the effects of recombinant IL-13 on the phenotype and function of synovial fluid (SF) macrophages and T cells derived from patients with rheumatoid **arthritis** (RA). Methods. The presence of IL-13 in SF was studied using an IL-13-specific enzyme-linked immunosorbent assay (ELISA); the production of IL-13 was studied in SF mononuclear cells (SFMC) by reverse transcriptase-polymerase chain reaction. The effects of recombinant IL-13 on cytokine production by and phenotype of SFMC were evaluated using cytokine- specific ELISAs and flow cytometry, respectively. The effect of IL-13 on the proliferation of SFMC was determined by 3H-thymidine incorporation. The production and the effects of IL-13 were compared with those of IL-4. Results. IL-13 was present in 27 of 28 SF samples, and IL-13 messenger RNA (mRNA) was detectable in SFMC. Importantly, IL-13 levels were significantly higher than those of IL-4, and IL-13 protein and mRNA were expressed in several samples, although IL-4 synthesis was undetectable. Recombinant IL-13 significantly reduced the production of IL-1.beta. and tumor necrosis factor a and the expression of CD16 and CD64 by SF macrophages, whereas the expression of HLA-DR and **CD23** was increased. These effects on SF macrophages were similar to those observed with IL-4, but in contrast to IL-4, IL-13 had no growth-promoting effect on SF T cells. Conclusion. IL-13 is consistently present in rheumatoid synovium. The ability of exogenous IL-13 to decrease the production of proinflammatory cytokines by SFMC suggests that it may have therapeutic potential in the **treatment** of patients with RA.

L30 ANSWER 6 OF 8 SCISEARCH COPYRIGHT 2003 ISI (R)
95:735643 The Genuine Article (R) Number: RX684. **TREATMENT** WITH **ANTIBODIES** TO **CD23** MARKEDLY AMELIORATES AN ESTABLISHED COLLAGEN-INDUCED **ARTHRITIS** IN MICE. PLATERZYBERK C (Reprint); BONNEFOY J Y. GLAXO IMB, DEPT IMMUNOL, CH-1228 GENEVA, SWITZERLAND. ARTHRITIS AND RHEUMATISM (SEP 1995) Vol. 38, No. 9, Supp. S, pp. 942. ISSN: 0004-3591. Pub. country: SWITZERLAND. Language: ENGLISH.

L30 ANSWER 7 OF 8 MEDLINE
96071560 Document Number: 96071560. PubMed ID: 7585180. Marked amelioration of established collagen-induced **arthritis** by **treatment** with **antibodies** to **CD23** in vivo.
Plater-Zyberk C; Bonnefoy J Y. (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland.) NATURE MEDICINE, (1995 Aug) 1 (8) 781-5. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB **CD23** is a low-affinity receptor for immunoglobulin E (IgE) expressed by a variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. **CD23** regulates many functional aspects of

immune cells, both in its cell-associated and soluble forms. In view of the increased levels of **CD23** in rheumatoid **arthritis**, we have studied the effect of neutralizing **CD23** in type II collagen-induced **arthritis** in mice, a model for human rheumatoid **arthritis**. Successful disease modulation is achieved by **treatment** of arthritic DBA/1 mice with either polyclonal or monoclonal **antibodies** to mouse **CD23**. Treated mice show a dose-related amelioration of **arthritis** with significantly reduced clinical scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decrease in cellular infiltration of the synovial sublining layer and limited destruction of cartilage and bone is evident in animals treated with therapeutic doses of anti-**CD23** **antibody**. These findings demonstrate the involvement of **CD23** in a mouse model of human rheumatoid **arthritis**.

L30 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1995:521449 Document No.: PREV199598535749. **Treatment** with **antibodies** to **CD23** markedly ameliorates an established collagen-induced **arthritis** in mice. Plater-Zyberk, Christine; Bonnefoy, Jean-Yves. Glaxo IMB, Immunol. Dep., 14 Chemin Des Aulx, CH-1228 Geneva Switzerland. Arthritis & Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S310. Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals San Francisco, California, USA October 21-26, 1995 ISSN: 0004-3591. Language: English.

=> s l28 and lupus erythematosus
L31 7 L28 AND LUPUS ERYTHEMATOSUS

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L32 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.
AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L32 ANSWER 2 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2001274349 EMBASE Low-grade non-Hodgkin's lymphoma in a patient with systemic **lupus erythematosus**. Robak T.; Robak E.; Bartkowiak J.; Blonski J.Z.; Niewiadomska H.; Wawrzyniak E.. Prof. T. Robak, Department of Hematology, Medical Univ. of Lodz, Copernicus Memorial Hospital, ul. Pabianicka 62, 93-513 Lodz, Poland. robaktad@psk2.am.lodz.pl. Leukemia and Lymphoma 41/5-6 (659-667) 2001.
Refs: 30.

ISSN: 1042-8194. CODEN: LELYEA. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Coexistence of systemic **lupus erythematosus** (SLE) with low-grade non-Hodgkin's lymphoma (LGNHL) has been described occasionally in the literature with the potential pathogenetic role of monoclonal B CD5+/CD19+ cells. We report a case of LGNHL which developed 18 months after diagnosis of SLE. The monoclonal population of lymphocytes in the peripheral blood and bone marrow was CD5/CD19 negative but CD19/CD22 positive. The SLE responded well to **treatment** with prednisone and the course of the LGNHL was stable and cytotoxic **treatment** was not required.

L32 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS

1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L32 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

1998:6398 Document No.: PREV199800006398. Study of expression of **CD23** on peripheral blood mononuclear cells in patients systemic **lupus erythematosus**. Li, Xiqing; Ling, Shaoxian; Wang, Bin. Dep. Dermatol., Sun Yat-Sen Meml. Hosp., Sun Yat-Sen Univ. Med. Sci., Guangzhou 510120 China. Zhonghua Pifuke Zazhi, (Oct., 1997) Vol. 30, No. 5, pp. 324-326. ISSN: 0412-4030. Language: Chinese. Summary Language: Chinese; English.

AB In order to study the relationship between expression of **CD23** on B cells and the development of SLE, and possible role in the pathogenesis of SLE, we used ABC immunohistochemistry and Northern dot-blot hybridization technique to detect **CD23** protein and mRNA expression on PBMC in SLE patients and healthy controls. The results showed: **CD23** protein and mRNA expression was significantly higher in active SLE patients than those in controls ($P<0.01$), and showed positive linear correlation between **CD23** expression and disease activity ($rs = 0.3814, P<0.05$), but there was no significant difference between the patients after **treatment** in comparison with controls ($P>0.05$). There were no significant difference ($P>0.05$) in the expression of **CD23** protein on PBMC among active SLE patients with different levels of ANA or dsDNA **antibody**, with or without renal or brain involvement as well as treated with corticosteroids and/or other immunosuppressants. It was implicated that abnormal activation and proliferation of B cells lead to over expression of **CD23** protein and mRNA in active SLE, but there was not direct relationship between over expression of **CD23** and the levels of ANA or anti-dsDNA **antibody**.

L32 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS

1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L32 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the **treatment** of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative **treatment** of mice against arthritis using monoclonal anti-**CD23 antibody, CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L32 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS

1993:493523 Document No. 119:93523 Murine and human cytokine (CD40-L) which binds to CD40, and soluble CD40 and CD40 fusion molecules. Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K. (Immunex Corp., USA). PCT Int. Appl. WO 9308207 A1 19930429, 79 pp. DESIGNATED STATES: W: AU, CA, FI, JP, KR, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US8990 19921023. PRIORITY: US 1991-783707 19911025; US 1991-805723 19911205.

AB The title CD40-L mols. are disclosed, as are related DNA sequences, vectors, and transformed host cells. The murine and human CD40-L polypeptides bind to the extracellular binding region of a CD40 receptor. Also provided are a CD40/IgG1 Fc region fusion protein and a sol. CD40 protein (sCD40) comprising the extracellular portion of CD40; both the CD40/Fc and sCD40 can inhibit CD40-L or anti-CD40 monoclonal **antibody**-induced B-cell stimulation, interleukin-4-induced IgE stimulation, and interleukin-4-induced **CD23** induction in

B-cells. Construction is described of a CD40/Fc DNA for prodn. of a fusion protein for use in detecting cDNA clones encoding a CD40 ligand. Also described are selection of a cell line putatively expressing CD40-L, prepn. of a cDNA library for expression cloning of murine CD40-L, cross-species hybridization methodol. used to isolate a human CD40-L homolog, anti-allergy therapeutic effects of sCD40 and CD40/Fc fusion protein, etc. Interaction of CD40 with its ligand was evidently the principal mol. interaction responsible for T-cell contact-dependent induction of B-cell growth and differentiation to both antigen-specific **antibody** prodn. and polyclonal Ig secretion.

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=> s l28 and multiple sclerosis
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L35 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.
AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L35 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.
AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L35 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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L35 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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L35 ANSWER 5 OF 5 SCISEARCH COPYRIGHT 2003 ISI (R)
96:382967 The Genuine Article (R) Number: UK211. LYMPHOCYTE SUBPOPULATION IN THE PERIPHERAL-BLOOD AND CEREBROSPINAL-FLUID OF PATIENTS WITH **MULTIPLE-SCLEROSIS**. HAVRDOVA E (Reprint); MARECKOVA H; JEDLICKA P; HANA I. IPVZ FTN, NEUROL KLIN, PRAGUE, CZECH REPUBLIC; ODDELENI KLIN IMUNOL FP 2, PRAGUE, CZECH REPUBLIC; IKEM, PRAGUE, CZECH REPUBLIC. CESKA A SLOVENSKA NEUROLOGIE A NEUROCHIRURGIE (1996) Vol. 59, No. 2, pp. 83-89. ISSN: 0301-0597. Pub. country: CZECH REPUBLIC. Language: Czech.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The structural basis of **multiple sclerosis** are perivascular inflammatory foci in the white matter of the CNS. In the development of these foci participate to a major extent lymphocytes which express various surface signs (CD markers). They pass from the peripheral

blood into the compartment of the CNS, produce various anti-inflammatory factors, mediate the destruction of myelin. The surface markers of lymphocytes can be detected by means of monoclonal **antibodies**, two signs concurrently can be examined by means of a flow cytometer. The objective of the present study was examination of lymphocyte subpopulations in the peripheral blood and cerebrospinal fluid in patients with exacerbation of **multiple sclerosis** during secondary progression and in patients with lumboischiadic syndrome (LS) and to assess the dynamics in relation to **treatment** with methylprednisolone and cytosine arabinoside in patients with **multiple sclerosis**. After elaboration of the method for examination of CD markers in lymphocytes in the CSF the authors found an increased ratio of CD3+, CD4+, CD8+ and CD57+ cells in CSF and a drop after **treatment** with methylprednisolone, furthermore a reduced ratio of CD4+CD45RA+ cells in CSF and a rise of these cells after **treatment**. In the peripheral blood a lower percentage of CD8+CD57+ cells and decline of the percentage of CD57+ cells after **treatment** was found. The percentage of CD28+ cells in patients with **multiple sclerosis** is permanently elevated, after **treatment** with methylprednisolone a rise of CD8+CD281, CD191 and **CD23**+ cells occurs; there is a decline of NK cells and CD19+CD5 cells. The other examined subpopulations did not differ in the investigated groups. The assessed abnormalities in CSF and in the peripheral blood support the idea of a persistent inflammatory activation in the compartment of the CNS as well as in the peripheral bloodstream of patients also in the initial years of secondary chronic progression of **multiple sclerosis**.

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L37 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L37 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,

PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L37 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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L39 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS

2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns **treatment** of autoimmune diseases

with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L39 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.
AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L39 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
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L39 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
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L41 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.
AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L41 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2003 ACS
2000:535179 Document No. 133:149142 Production of tetravalent **antibodies**. Braslawsky, Gary Ronald; Hanna, Nabil; Hariharan, Kandasamy; Labarre, Michael J.; Huynh, Tri B. (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2000044788 A1 20000803, 65 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US1893 20000128. PRIORITY: US 1999-238741 19990128.
AB The present invention relates to a novel process for the prepn. of biol. active **antibody** dimers in a pharmaceutically acceptable compn. The homodimer may be anti-CD20 homodimer or anti-**CD23** homodimer. The dimers can be composed of two **antibody** mols. having the same antigen binding specificity and linked through a reducible, disulfide, or a non-reducible thioether, bond (homodimer). Alternatively, the dimers can be composed of two different **antibody** mols. having binding specificity for two distinct antigens (heterodimer). These dimers are

useful for inducing hyper-crosslinking of membrane antigens. The present invention further relates to the use of biol. active **antibody** dimers for the preferential killing or inhibition of selected cell populations in the **treatment** of diseases such as cancer, allergic disease or autoimmune disorders.

L41 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.
AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L41 ANSWER 4 OF 16 MEDLINE
1998202080 Document Number: 98202080. PubMed ID: 9543080. Changes in **CD23** expression of blood and skin in atopic eczema after Chinese herbal therapy. Banerjee P; Xu X J; Poulter L W; Rustin M H. (Department of Dermatology, Royal Free Hospital School of Medicine, London, UK.) CLINICAL AND EXPERIMENTAL ALLERGY, (1998 Mar) 28 (3) 306-14. Journal code: 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.
AB BACKGROUND: Aberrant expression of **CD23** (low affinity IgE receptor) on cells of the monocyte/macrophage series in peripheral blood and lesional skin of patients with atopic eczema has been demonstrated. It is not known whether this abnormality results from a fundamental systemic problem of the monocytes of these patients or reflects local changes to cell populations within the skin tissues. OBJECTIVES: This study was designed to determine whether this aberrant expression was caused by local cutaneous influences on mature cells or fundamental changes in monocyte differentiation. The possible relationship between these aberrations and clinical severity was also investigated by repeating these immunopathological studies after a course of efficacious **treatment** with Chinese herbal therapy (CHT). METHODS: Peripheral blood mononuclear cells were obtained from patients with atopic eczema before, and after 8 weeks of **treatment**. Efficacy of CHT was quantified on clinical grounds. Monocytes were isolated by adherence to plastic and cultured for up to 7 days. Samples were harvested at 2, 5 and 7 days of culture and cytospins prepared. Immunocytochemical staining to identify phenotypic subsets was performed on the monocytes at time 0 and on maturing cells from culture. This immunocytology was quantified using computerized image analysis equipment to determine the emergence of macrophage subsets and their level of **CD23** expression. Biopsies were taken from lesional skin before and after **treatment** and immunohistology was performed on cryostat sections to determine the number of antigen presenting cells expressing **CD23** as well as the level of expression of these molecules. RESULTS: The results showed that increased numbers of monocytes from patients with atopic eczema express **CD23** at day 0 and that cultured monocytes from these patients

differentiate faster during the 7 day culture period as compared to normal controls. Efficacious **treatment** did not affect the number of peripheral blood monocytes expressing **CD23**. However, **treatment** did lead to a significant decrease in the number of **CD23**+ mature macrophages in the skin as well as a reduction in the level of expression of this moiety. These results demonstrate that changes in clinical severity are more closely related to the expression of **CD23** on mature antigen presenting cells in lesional skin rather than to differentiating peripheral blood monocyte **CD23** expression. CONCLUSIONS: These results suggests that local factors within lesional skin govern the accumulation and the expression of **CD23** on mature macrophages and that these factors may be more relevant to the pathogenesis of the disease than aberrations in **CD23** expression that may occur systemically.

L41 ANSWER 5 OF 16 MEDLINE

97188350 Document Number: 97188350. PubMed ID: 9036935. The high-affinity receptor for IgE is the predominant IgE-binding structure in lesional skin of atopic **dermatitis** patients. Klubal R; Osterhoff B; Wang B; Kinet J P; Maurer D; Stingl G. (Department of Dermatology, University of Vienna Medical School, Austria.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1997 Mar) 108 (3) 336-42. Journal code: 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB While the skin of most patients with atopic **dermatitis** (AD) is known to contain IgE-bearing cells, the contribution of the various IgE-binding structures to this phenomenon is not fully understood. To address this issue, we eluted cell-bound IgE from cryostat sections of lesional AD skin by acid **treatment** and performed reconstitution experiments with IgE in the absence or presence of reagents directed against the currently known IgE-binding structures. We found that incubation of acid-treated sections, with either chimeric or serum IgE, resulted in the appearance of sizable numbers of anti-IgE-reactive cells. This cellular IgE loading could be entirely prevented by preincubation of the sections with the anti-Fc epsilonRI alpha MoAb 15-1 but not with either **antibodies** against Fc epsilonRII/**CD23** and Fc gammaRII/CD32 or with alpha-lactose. To exclude the possibility that acid **treatment** of tissue sections may have adversely influenced the IgE-binding capacity of IgE receptors other than Fc epsilonRI, we performed an identical series of experiments on AD skin samples that, as an exception, were essentially devoid of anti-IgE-reactive cells. Again, no IgE loading was detected when these sections were preincubated with anti-Fc epsilonRI alpha MoAbs. In contrast, preincubation of the sections with alpha-lactose and/or MoAbs against Fc epsilonRII/**CD23** or Fc gammaRII/CD32 did not affect IgE loading. Together with the observations that anti-Fc epsilonRI alpha-reactive and IgE-binding cells are largely overlapping populations and include cells of the Langerhans cell/dendritic cell lineage, mast cells, and a few dermal dendrocytes and eosinophils, our results demonstrate that Fc epsilonRI is the predominant and, perhaps, the only biologically relevant IgE-binding structure on histogenetically and functionally diverse cell populations of AD skin.

L41 ANSWER 6 OF 16 MEDLINE

97191337 Document Number: 97191337. PubMed ID: 9039295. Modulation by Chinese herbal therapy of immune mechanisms in the skin of patients with atopic eczema. Xu X J; Banerjee P; Rustin M H; Poulter L W. (Department of Dermtology, Royal Free Hospital and School of Medicine, London, UK.) BRITISH JOURNAL OF DERMATOLOGY, (1997 Jan) 136 (1) 54-9. Journal code: 0004041. ISSN: 0007-0963. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Ten patients with atopic eczema (AE) received **treatment** with Chinese herbal therapy (CHT; Zemaphyte) for 2 months. The severity of the eczema was recorded and skin biopsies were taken from lesional (L) and non-lesional (NL) skin before and after **treatment**. The skin

biopsies were stained to detect T-cell subsets (CD4, CD8, CD45Ro and CD25), macrophage subsets (RFD7), dendritic cells (RFD1). Langerhans cells (CD1), HLA-DR, low-affinity IgE receptors (**CD23**) and high-affinity IgE receptors (15A5, 22H7). A quantitative assessment of the numbers of positively stained cells was made. Monoclonal **antibody** binding specifically to **CD23**(Fc epsilon RII) was used, in combination with cell subset monoclonal **antibodies** to quantify the cellular distribution of **CD23** antigen in the skin. Following 2 months of **treatment** with CHT, erythema was reduced by 53%. There was also a significant reduction in HLA-DR expression. The numbers of RFD1 + **CD23** +, RFD7 + **CD23** +, CD1 + **CD23**+ and CD25 + cells in lesional skin decreased significantly after **treatment** (RFD1 + **CD23** + from 0.39 to 0.21, RFD7 + **CD23** + from 0.29 to 0.16. CD1 + **CD23** + from 0.24 to 0.09, CD25 + from 0.84 to 0.31 in epidermis and from 1.62 to 0.94 in dermis (mean cells numbers per unit area). No significant change in cell numbers in NL skin or expression of Fc epsilon RI in either L or NL samples was observed after **treatment**. This study confirms that CHT is clinically efficacious and that clinical improvement is associated with a significant reduction in antigen-presenting cells expressing **CD23**.

L41 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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L41 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the **treatment** of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative **treatment** of mice against arthritis using monoclonal anti-**CD23 antibody, CD23**

-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L41 ANSWER 9 OF 16 MEDLINE

96184215 Document Number: 96184215. PubMed ID: 8620093. Association of immunological changes with clinical efficacy in atopic eczema patients treated with traditional Chinese herbal therapy (Zemaphyte). Latchman Y; Banerjee P; Poulter L W; Rustin M; Brostoff J. (Department of Immunology, UCL Medical School, London, UK.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1996 Mar) 109 (3) 243-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB The efficacy of the Chinese herbal therapy (Zemaphyte) has been well established as a **treatment** for atopic eczema (AE) in clinical trials. The purpose of this study was to probe the immunological changes that occurred when patients were treated with the herbs for a period of 8 weeks. This **treatment** decreased serum IgE complexes (p less than 0.05) but did not affect total serum IgE or **CD23** expression on peripheral blood monocytes. Peripheral blood mononuclear cells from patients before and after **treatment** were cultured overnight with interleukin 4 and the ability of this cytokine to induce **CD23** on monocytes from treated patients was found to be significantly diminished (p less than 0.01). Soluble interleukin 2 receptor and soluble vascular cell adhesion molecule were both raised in the serum of AE patients compared to control individuals. Both these parameters were decreased following **treatment** (p less than 0.05). All these changes coincided with improvement in erythema and surface damage scores. There was no alteration in soluble intracellular adhesion molecule or soluble **CD23**. The results of these investigations would suggest that this herbal **treatment** has the ability to target various immunological parameters which may be involved in the pathogenesis of AE.

L41 ANSWER 10 OF 16 SCISEARCH COPYRIGHT 2003 ISI (R)

95:786713 The Genuine Article (R) Number: TD446. PITYROSPORUM-OVALE EXTRACTS INCREASE INTERLEUKIN-4, INTERLEUKIN-L0 AND IGE SYNTHESIS IN PATIENTS WITH ATOPIC ECZEMA. KROGER S; NEUBER K (Reprint); GRUSECK E; RING J; ABECK D. UNIV HAMBURG, HOSP EPPENDORF, DEPT DERMATOL & ALLERGOL, MARTINISTR 52, D-20246 HAMBURG, GERMANY (Reprint); UNIV HAMBURG, HOSP EPPENDORF, DEPT DERMATOL & ALLERGOL, D-20246 HAMBURG, GERMANY. ACTA DERMATO-VENEREOLOGICA (SEP 1995) Vol. 75, No. 5, pp. 357-360. ISSN: 0001-5555. Pub. country: GERMANY. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Evidence for a possible role of the lipophilic yeast Pityrosporum ovale in the pathophysiology of atopic eczema has been found both in laboratory and therapeutical studies. Positive type I prick test reactions to P. ovale correlate with the intensity of eczematous skin lesions in the head and neck regions of patients with atopic eczema, Furthermore, antifungal **treatment** has been shown to be helpful in atopic eczema, In the present study the effect of P. ovale on IgE synthesis and cytokine production (IL-2, IFN gamma, IL-4, IL-10) was investigated in patients with atopic eczema, in vitro. Eight patients with atopic eczema were studied; of these, 5 patients had specific IgE **antibodies** against P. ovale, as determined by fluoroimmunoassay (EAST). The control group consisted of 5 healthy non-atopic, P. ovale IgE-**antibody** -negative volunteers. Freshly isolated peripheral blood mononuclear cells (PBMC) were incubated in the presence of different antigen concentrations (0.01, 0.1, 1.0, 10 mu g/l x 10(6) cells) of P. ovale. IgE contents in the cell culture supematants were significantly elevated in RAST(+) patients with atopic eczema ($p<0.05$), compared with RAST(-) atopic eczema patients and healthy volunteers, Coincubation of P. ovale-stimulated PBMC with IL-4

(50 U/l/ 1x10(6) cells) resulted in a significantly higher IgE synthesis only in the RAST(+) atopic eczema patients, Additionally, incubation of PBMC from RAST(+) patients with atopic eczema led to an elevated synthesis of the T(H)2 related cytokines IL-4 and IL-10. Within the atopic eczema group, two subgroups differed markedly in their response to P. ovale antigen stimulation with a good correlation to the presence of specific IgE in serum and in vitro IL-4 and IL-10 production, The data support the assumption that P. ovale antigens might play a role in skin inflammation in at least a subgroup of patients with atopic eczema characterized by the presence of specific IgE **antibodies** to P. ovale.

L41 ANSWER 11 OF 16 MEDLINE
94165514 Document Number: 94165514. PubMed ID: 7509836. DNFB contact sensitivity (CS) in BALB/c and C3H/He mice: requirement for early-occurring, early-acting, antigen-specific, CS-initiating cells with an unusual phenotype (Thy-1+, CD5+, CD3-, CD4-, CD8-, sIg-, B220+, MHC class II-, **CD23**+, IL-2R-, IL-3R+, Mel-14-, Pgp-1+, J11d+, MAC-1+, LFA-1+, and Fc gamma RII+). Ishii N; Takahashi K; Nakajima H; Tanaka S; Askenase P W. (Department of Dermatology, Yokohama City University School of Medicine, Japan.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1994 Mar) 102 (3) 321-7. Journal code: 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB Immunization of mice for contact sensitivity induces two different antigen-specific Thy-1+ cell activities that are required to act in sequence for elicitation of contact sensitivity. In this study, 2,4-dinitro-1-fluorobenzene contact sensitivity responses in BALB/c and C3H/He mice demonstrated the importance of early-acting and antigen-specific contact sensitivity-initiating cells to recruit the classical, late-acting contact sensitivity effector T cells. Employing in vitro **treatment** of sensitized cells with monoclonal **antibodies** to cell surface determinants and then incubation in complement, prior to adoptive cell transfer, the contact sensitivity-initiating cells were shown to have a surface phenotype that is quite unusual for antigen-specific cells [Thy-1+, CD5+, CD3-, CD4-, CD8-, sIg-, B220+, major histocompatibility complex class II-, **CD23**+, IL-2R-, IL-3R+, Mel-14-, CD44+ (Pgp-1+), J11d+ (HSA+), MAC-1+, LFA-1+, and Fc gamma IIR+], and is quite different from the late-acting, contact sensitivity-effector T cells (Thy-1+, CD5+, CD3+, CD4+, CD8-, sIg-, B220-, major histocompatibility complex class II-, **CD23**-, IL-2R+, IL-3R-, and CD44- (Pgp-1-), J11d-(HSA-), MAC-1-, LFA-1+, Fc gamma IIR-). Contact sensitivity initiation was required for elicitation of late 24-h 2,4-dinitro-1-fluorobenzene contact sensitivity responses, in both BALB/c and C3H/He mice. Moreover, relatively high doses of some monoclonal **antibodies** [anti-B220 (CD45RA) and anti-**CD23** (IgE Fc epsilon II receptor)] were necessary to completely eliminate all contact sensitivity-initiating cells that permitted expression of late contact sensitivity-effector T-cell activity. In contrast, high doses of monoclonal **antibody** specific for surface determinants of late-acting contact sensitivity effector T cells (anti-CD3 and anti-CD4), when used in high doses similar to anti-B220 and anti-**CD23**, had no effect on contact sensitivity-initiating cell activity. Our results indicate that two very different antigen-specific Thy-1+ cells are necessary to elicit 2,4-dinitro-1-fluorobenzene contact sensitivity in BALB/c and C3H/He mice.

L41 ANSWER 12 OF 16 SCISEARCH COPYRIGHT 2003 ISI (R)
93:137161 The Genuine Article (R) Number: KP495. ATOPIC-**DERMATITIS** - CORRELATION OF PERIPHERAL-BLOOD T-CELL ACTIVATION, EOSINOPHILIA AND SERUM FACTORS WITH CLINICAL SEVERITY. WALKER C (Reprint); KAGI M K; INGOLD P; BRAUN P; BLASER K; BRUIJNZEELKOOMEN C A F M; WUTHRICH B. SWISS INST ALLERGY & ASTHMA RES, SIAF, OBERESTR 22, CH-7270 DAVOS, SWITZERLAND (Reprint); ZURCHER HOCHGEBIRGSKLIN, DAVOS, SWITZERLAND; UNIV HOSP ZURICH, DEPT DERMATOL, ALLERGY UNIT, CH-8091 ZURICH, SWITZERLAND. CLINICAL AND

EXPERIMENTAL ALLERGY (FEB 1993) Vol. 23, No. 2, pp. 145-153. ISSN: 0954-7894. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In the first part of this study peripheral blood lymphocyte subpopulations, their activation state and various serum parameters were measured in extrinsic and intrinsic atopic **dermatitis** (AD) patients compared to normal individuals. Beside the characteristic eosinophilia, significantly increased numbers of CD4+ T cells with increased expression of IL-2 receptors (IL-2R) and HLA-DR were noted in the AD patients. In addition, extrinsic AD patients showed increased numbers of **CD23**+ B cells and decreased numbers of CD16+ natural killer cells. Moreover, increased serum levels of eosinophil cationic protein (ECP) and soluble IL-2R as well as soluble factors that prolong survival of eosinophils in vitro could be demonstrated. In the second section of this study we determine how these blood immunological parameters relate to the clinical severity of the skin lesions of AD, by weekly analysis of 12 AD patients attending a high altitude clinic for 3 to 6 weeks. The patients were divided into two groups on the basis of **treatment** with topical steroids, but during the observation period a significant improvement in clinical status was observed in all AD patients independent of topical steroid therapy. A progressive decrease in eosinophil and activated T cell numbers, soluble IL-2R levels and serum eosinophil survival prolonging activity could be demonstrated, which closely correlated with the clinical severity of the AD.

L41 ANSWER 13 OF 16 SCISEARCH COPYRIGHT 2003 ISI (R)
92:582713 The Genuine Article (R) Number: JQ368. REGULATORY ROLE OF CYTOKINES IN IGE-MEDIATED ALLERGY. TAN H P (Reprint); LEBECK L K; NEHLSENCANNARELLA S L. LOMA LINDA UNIV, SCH MED, DEPT SURG, CTR IMMUNOL, LOMA LINDA, CA, 92354 (Reprint); LOMA LINDA UNIV, SCH MED, DEPT MICROBIOL, LOMA LINDA, CA, 92354; LOMA LINDA UNIV, SCH MED, DEPT SURG, LOMA LINDA, CA, 92354; LOMA LINDA UNIV, SCH MED, DEPT PATHOL, LOMA LINDA, CA, 92354. JOURNAL OF LEUKOCYTE BIOLOGY (JUL 1992) Vol. 52, No. 1, pp. 115-118. ISSN: 0741-5400. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The discovery of immunoglobulin E (IgE) is considered the most important contribution, to date, in the field of clinical allergy. Studies in rodents and humans have suggested that IgE production could be regulated by antigen-specific helper and suppressor T cells and by isotype-specific factors having affinity for IgE. In recent years, the synthesis of IgE has been shown to be regulated, in part, by a cytokine network. This review summarizes the cytokines that up-regulate (interleukins-4, 5, and 6) and down-regulate (interferon-gamma and interleukin-2) the production of IgE. Emphasis is placed on IL-4 and IFN-gamma, two lymphokines known to play a major, but reciprocal, role in IgE synthesis. Increased insight into the various mechanisms of IgE control by cytokines and their receptors will eventually lead to improved **treatment** strategies in the clinical management of IgE-mediated allergy.

L41 ANSWER 14 OF 16 MEDLINE
91223680 Document Number: 91223680. PubMed ID: 1673878. Fc epsilon receptor II/**CD23**-positive lymphocytes in atopic **dermatitis**. I. The proportion of Fc epsilon RII+ lymphocytes correlates with the extent of skin lesion. Takigawa M; Tamamori T; Horiguchi D; Sakamoto T; Yamada M; Yoshioka A; Toda K; Imamura S; Yodoi J. (Department of Dermatology, Hamamatsu University School of Medicine, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 May) 84 (2) 275-82. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Cells expressing Fc receptors for IgE (Fc epsilon RII) were identified in the peripheral blood from patients with atopic **dermatitis** and with eczematous **dermatitis**, and normal non-atopic subjects by

using monoclonal **antibodies** to human lymphocyte Fc epsilon RII, and to lymphoid cell-surface antigens by immunofluorescence staining. Based on the extent of the **dermatitis** patients were classified as severe (greater than 50% skin surface involved), moderate (50-10%) and mild (less than 10%). Patients with severe and moderate atopic **dermatitis** had 5.9% and 5.7% Fc epsilon RII+ peripheral blood mononuclear cells (PBMC), respectively, that were significantly higher than percentages in mild atopic **dermatitis** patients (2.6%), severe to moderate eczematous **dermatitis** patients (2.3%), mild eczematous **dermatitis** patients (2.2%) and normal individuals (1.7%)(0.05 greater than P). In severe and moderate atopic **dermatitis** patients, 10% of Fc epsilon RII+ PBMC were T cells that preferentially expressed CD8, and the remainder B cells and monocytes. Fc epsilon RII+ T cells comprised 1% of peripheral T cells, while half or more of peripheral B cells expressed Fc epsilon RII. In mild atopic **dermatitis** patients, eczematous **dermatitis** patients and normal subjects. Fc epsilon RII were expressed exclusively on 25-35% of peripheral B cells. Short-term **treatment** and long-term follow-up of atopic **dermatitis** patients revealed that changes in the skin condition were related closely to fluctuations in the proportion of Fc epsilon RII+ PBMC. Total serum IgE levels and atopic respiratory allergy did not influence the percentage of Fc epsilon RII+ PBMC. These findings suggest that the percentage of Fc epsilon RII+ PBMC reflects the extent of atopic **dermatitis**.

L41 ANSWER 15 OF 16 SCISEARCH COPYRIGHT 2003 ISI (R)
91:264949 The Genuine Article (R) Number: FJ463. FC-XI RECEPTOR-II/**CD23**-POSITIVE LYMPHOCYTES IN ATOPIC-**DERMATITIS** .1. THE PROPORTION OF FC-XI-RII+ LYMPHOCYTES CORRELATES WITH THE EXTENT OF SKIN LESION. TAKIGAWA M (Reprint); TAMAMORI T; HORIGUCHI D; SAKAMOTO T; YAMADA M; YOSHIOKA A; TODA K; IMAMURA S; YODOI J. HAMAMATSU UNIV, SCH MED, DEPT DERMATOL, HAMAMATSU, SHIZUOKA 431-31, JAPAN (Reprint); KYOTO UNIV, SCH MED, DEPT DERMATOL, KYOTO 606, JAPAN; KYOTO UNIV, INST IMMUNOL, KYOTO 606, JAPAN. CLINICAL AND EXPERIMENTAL IMMUNOLOGY (1991) Vol. 84, No. 2, pp. 275-282. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cells expressing Fc receptors for IgE (Fc-epsilon-RII) were identified in the peripheral blood from patients with atopic **dermatitis** and with eczematous **dermatitis**, and normal non-atopic subjects by using monoclonal **antibodies** to human lymphocyte Fc-epsilon-RII, and to lymphoid cell-surface antigens by immunofluorescence staining. Based on the extent of the **dermatitis** patients were classified as severe (> 50% skin surface involved), moderate (50-10%) and mild (> 10%). Patients with severe and moderate atopic **dermatitis** had 5.9% and 5.7% Fc-epsilon-RII+ peripheral blood mononuclear cells (PBMC), respectively, that were significantly higher than percentages in mild atopic **dermatitis** patients (2.6%), severe to moderate eczematous **dermatitis** patients (2.3%), mild eczematous **dermatitis** patients (2.2%) and normal individuals (1.7%) (0.05 > P). In severe and moderate atopic **dermatitis** patients, 10% of Fc-epsilon-RII+ PBMC were T cells that preferentially expressed CD8, and the remainder B cells and monocytes. Fc-epsilon-RII+ T cells comprised 1% of peripheral T cells, while half or more of peripheral B cells expressed Fc-epsilon-RII. In mild atopic **dermatitis** patients, eczematous **dermatitis** patients and normal subjects, Fc-epsilon-RII were expressed exclusively on 25-35% of peripheral B cells. Short-term **treatment** and long-term follow-up of atopic **dermatitis** patients revealed that changes in the skin condition were related closely to fluctuations in the proportion of Fc-epsilon-RII+ PBMC. Total serum IgE levels and atopic respiratory allergy did not influence the percentage of Fc-epsilon-RII+ PBMC. These findings suggest that the percentage of Fc-epsilon-RII+ PBMC reflects the extent of atopic **dermatitis**.

L41 ANSWER 16 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
91353239 EMBASE Document No.: 1991353239. Itch and atopic **dermatitis** : Clinical and experimental studies. Wahlgren C.-F.. Department of Dermatology, Karolinska Hospital, Karolinska Institute,Stockholm, Sweden. Acta Dermato-Venereologica, Supplement -/165 (4-53) 1991.
ISSN: 0365-8341. CODEN: AVSUAR. Pub. Country: Norway. Language: English. Summary Language: English.

AB The aims of the study were to develop and evaluate methods for quantitative measurement of itch, to investigate the perception of itch in patients with atopic **dermatitis** (AD), and to measure itch in such patients during **treatment** with H1-receptor antagonists or cyclosporin A, thereby exploring possible mechanisms in the pathogenesis of itch in AD. In a double-blind, randomized, placebo-controlled, cross-over study of 30 AD patients using a potent, topical, antipruritic corticosteroid, two methods for measuring itch both successfully detected the itch-relieving effect of the corticosteroid. The two methods comprised new portable data-loggers (Pain-Track) for continuous recording of itch, and conventional visual analogue scale (VAS) forms for retrospective recording. The main advantages of the Pain-Track method are possibilities for frequent sampling, surveillance of compliance, and analysis of a large amount of data. Induction and measurement of experimental histamine-induced itch were studied in 38 healthy subjects. It was shown that pruritic stimuli should be presented in a random order so as to avoid systematic errors in the perception of itch. Two rating scales, a seven-stepped non-verbal scale on a Pain-Track logger, and a 100-mm VAS on a potentiometer, were found valid for continuous recording of itch. The perception of experimental itch was studied in 32 AD patients and 32 healthy controls. The itch responses provoked by wool fibres were significantly stronger in AD patients than in controls, whereas the histamine-induced dose-response curves for itch did not differ significantly between the two groups, who discriminated equally well between weak and strong histamine stimuli. No increased skin mast cell releasability was shown in vivo to compound 48/80 in AD patients. Their itch responses to the different pruritic stimuli did not correlate with clinical itch intensity, eczema score or serum IgE-level. In a double-blind, randomized, placebo-controlled, cross-over study of 25 AD patients, the effect on clinical itch of a sedative (clemastine) and of a non-sedative (terfenadine) antihistamine did not differ from that of placebo, although both drugs had a pronounced H1-receptor-antagonizing effect in the skin and clemastine was significantly sedative. These findings support the view that histamine is not the major pruritogen in AD, and that sedation is not necessarily associated with itch relief. In a double-blind, randomized, placebo-controlled, cross-over study of 10 AD patients, 10 days' **treatment** with cyclosporin A (CSA), 5 mg/kg/day, significantly reduced itch intensity, eczema score and the number of peripheral blood eosinophils. Relapses were seen within 2-30 days of completion of CSA therapy. In at least 50% of the patients, CSA reduced the number of CD3+, CD4+, HLA-DR+, IgE+, **CD23**+ (low-affinity Fc-IgE receptor+), intercellular adhesion molecule-1+, and EG2+ (activated eosinophils) cells in lesional skin. The changes of itch magnitude in the patients did not strictly parallel any specific change in the occurrence of these cell surface markers. The mechanism of action for the antipruritic effect of CSA remains unclear, but it is hypothesized that cytokines may be involved in the pathogenesis of itch in AD.

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L43 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L43 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L43 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte

nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L43 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to **CD23** useful in the **treatment** of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative **treatment** of mice against arthritis using monoclonal anti-**CD23 antibody**, **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

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L44 4 L28 AND URTICARIA

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L45 ANSWER 1 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2003124852 EMBASE Technology evaluation: Omalizumab, Genentech/Novartis/Tanox. Lazaar A.L.. A.L. Lazaar, Univ. of PA Medical Center Pulmonary, Allergy and Critical Care Division, 421 Curie Boulevard, Philadelphia, PA 19104-6160, United States. alazaar@mail.med.upenn.edu. Current Opinion in Molecular Therapeutics 5/1 (81-89) 2003. ISSN: 1464-8431. CODEN: CUOTFO. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB Genentech, Novartis and Tanox have co-developed Genentech's anti-IgE humanized monoclonal **antibody** omalizumab for the **treatment** of allergic rhinitis and asthma. The **antibody** is currently undergoing phase II clinical trials for allergic rhinitis in Canada and phase III clinical trials for both indications in Japan. Omalizumab is at the pre-registration stage for both indications in the US, New Zealand, Switzerland and Western Europe, and is currently registered for both indications in Australia.

L45 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,

ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

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L45 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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=> s l28 and nephrotic syndrome

L46 3 L28 AND NEPHROTIC SYNDROME

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L47 3 DUP REMOVE L46 (0 DUPLICATES REMOVED)

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L47 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
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=> s l28 and glomerulonephritis
L48 5 L28 AND GLOMERULONEPHRITIS

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L49 5 DUP REMOVE L48 (0 DUPLICATES REMOVED)

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L49 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

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L49 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

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L49 ANSWER 3 OF 5 MEDLINE
97169074 Document Number: 97169074. PubMed ID: 9016881. Constitutive expression of interleukin (IL)-4 in vivo causes autoimmune-type disorders in mice. Erb K J; Ruger B; von Brevern M; Ryffel B; Schimpl A; Rivett K. (The Malaghan Institute of Medical Research, Department of Medicine, Wellington School of Medicine, New Zealand.) JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Jan 20) 185 (2) 329-39. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.
AB The transgenic (tg) expression of interleukin (IL)-4 under the control of a major histocompatibility complex (MHC) class I promoter leads to B cell hyperactivity in mice, characterized by increased B cell surface MHC class II and **CD23** expression, elevated responsiveness of the B cells to polyclonal ex vivo stimulation, and increased immunoglobulin (Ig)G1 and IgE serum levels. Tg mice develop anemia, **glomerulonephritis** with complement and immune deposition in the glomeruli, and show increased production of autoantibodies. **Treatment** of IL-4 tg mice with anti-IL-4 neutralizing **antibodies** protected the mice from disease development, showing that IL-4 was responsible for the observed disorders. Deletion of superantigen responsive autoreactive T cells in the IL-4 tg mice was normal and **treatment** of mutant mice with deleting anti-CD4 **antibodies** failed to ablate the onset of autoimmune-like disease, suggesting that CD4+ T cells were not the primary cause of the disorders. Furthermore, the deletion of B cells reacting against MHC class I molecules was also normal in the IL-4 tg mice. Therefore the most likely explanation for the increased production of autoantibodies and the autoimmunelike disorders is that IL-4 acts directly on autoreactive B cells by expanding them in a polyclonal manner. Taken together our results show that inappropriate multi-organ expression of IL-4 in vivo leads to autoimmune-type disease in mice.

L49 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
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L50 0 L28 AND INFLAMMATORY BOWEL DISEASE

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L51 4 L28 AND ULCERATIVE COLITIS

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=> s l28 and Crohn's disease
MISMATCHED QUOTE 'CROHN'S'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

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L53 0 L28 AND "CROHN'S DISASE"

=> s l28 and Sjogrens syndrome
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L55 3 L28 AND ALLERGIES

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L56 3 DUP REMOVE L55 (0 DUPLICATES REMOVED)

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L56 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
2003:100598 Document No. 138:219866 Immunological mechanisms of anti-IgE **treatment**. van Neerven, R. J. J.; van Roomen, C. P. A. A.; Knol, E. F. (Amsterdam, 1321, Neth.). New Trends in Allergy V, [International Symposium], 5th, Davos, Switzerland, Sept. 15-17, 2000, Meeting Date 2000, 284-291. Editor(s): Ring, Johannes; Behrendt, Heidrun. Springer-Verlag: Berlin, Germany. ISBN: 3-540-43082-2 (English) 2002. CODEN: 69DOXF.
AB A review. Non-anaphylactogenic anti-IgE mAb have been developed over the past decade to treat atopic **allergies**. These **antibodies** neutralize circulating IgE mols., and thus prevent IgE from binding to its receptors, Fc.epsilon.RI and **CD23**. Efficacy of anti-IgE **treatment** has been shown in several clin. trials, and new, unanticipated, mechanisms by which anti-IgE exerts its clin. effect are being discovered. Here the authors summarize a no. of studies on the immunol. mechanisms underlying anti-IgE **treatment**.

L56 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
2000:133697 Document No. 132:203144 Low-adenosine antisense oligonucleotide agents, compositions, kits and **treatments** for respiratory disorders. Nyce, Jonathan W. (East Carolina University, USA). PCT Int. Appl. WO 2000009525 A2 20000224, 1343 pp. DESIGNATED STATES: W: AU, CA, CN, MX, RU, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US17712 19990803. PRIORITY: US 1998-95212 19980803.
AB A compn. comprises a nucleic acid comprising an oligo antisense to a target such as polypeptide(s) assocd. with an ailment afflicting lung airways, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents. The agent of the invention may be prepd. by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more antisense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a universal base. The agent, compn. and formulations are used for prophylactic, preventive and therapeutic **treatment** of ailments assocd. with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasoconstriction, inflammation, **allergies**, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory

distress syndrome (ARDS), ischemic conditions including ischemia itself, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, pancreatic cancer, lung cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastasis, etc., as well as all types of cancers with may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present **treatment** is suitable for administration in combination with other **treatments**, e.g. before, during and after other **treatments**, including radiation, chemotherapy, **antibody** therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The **treatment** of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs. The invention is exemplified with specificity and pharmacokinetic studies using phosphorothioated antisense oligonucleotides targeted to the adenosine receptors A1, A2a, A2b, and A3.

L56 ANSWER 3 OF 3 MEDLINE
97276838 Document Number: 97276838. PubMed ID: 9130531. Demonstration of the therapeutic potential of non-anaphylactogenic anti-IgE **antibodies** in murine models of skin reaction, lung function and inflammation. Heusser C H; Wagner K; Bews J P; Coyle A; Bertrand C; Einsle K; Kips J; Eum S Y; Lefort J; Vargaftig B B. (Asthma Allergy Research Department, Ciba Geigy Ltd., Basel, Switzerland.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1997 May-Jul) 113 (1-3) 231-5. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.
AB BACKGROUND: **Allergies** and allergic asthma are believed to be mediated by allergen-specific IgE **antibodies**. We have investigated the therapeutic potential of inhibiting endogenous IgE by a non-anaphylactogenic anti-mouse IgE **antibody** 1-5 with respect to its effects on antigen-induced skin reaction, lung function changes and lung inflammation in mice. METHODS: Mice were immunized with benzylpenicillinoyl-KLH or ovalbumin, and antigen-mediated skin reaction, bronchoconstriction, bronchopulmonary hyperresponsiveness (BHR) and lung eosinophilic inflammation determined in anti-IgE 1-5-treated versus untreated animals. RESULTS: Application of anti-IgE 1-5 inhibited (by 90%) the serum IgE and, 3-4 days after onset of **treatment**, blocked the antigen-induced skin reaction. Furthermore, the **antibody** also inhibited (by 90%) the antigen-induced infiltration of eosinophils into the lung. This latter effect seems to be mediated by blocking the IgE-**CD23** interaction and indicates that lung eosinophilic inflammation also depends on IgE. Moreover, when applied to rats passively sensitized with mouse IgE, **antibody** 1-5 inhibited the antigen-induced bronchoconstriction. A similar effect could be seen in actively immunized mice, where **antibody** 1-5 was able to inhibit (by 70%) the ovalbumin-induced bronchoconstriction as well as BHR. CONCLUSIONS: In summary, non-anaphylactogenic anti-IgE **antibodies** can markedly inhibit IgE levels and IgE-mediated allergic reactions. Since bronchoconstriction, BHR and lung eosinophilic inflammation can be suppressed, such **antibodies** may be attractive principles for the **treatment** of allergic asthma.

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L58 ANSWER 1 OF 23 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2003124852 EMBASE Technology evaluation: Omalizumab, Genentech/Novartis/Tanox. Lazaar A.L.. A.L. Lazaar, Univ. of PA Medical Center Pulmonary, Allergy and Critical Care Division, 421 Curie Boulevard, Philadelphia, PA 19104-6160, United States. alazaar@mail.med.upenn.edu. Current Opinion in Molecular Therapeutics 5/1 (81-89) 2003.
ISSN: 1464-8431. CODEN: CUOTFO. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Genentech, Novartis and Tanox have co-developed Genentech's anti-IgE humanized monoclonal **antibody** omalizumab for the **treatment** of allergic rhinitis and **asthma**. The **antibody** is currently undergoing phase II clinical trials for allergic rhinitis in Canada and phase III clinical trials for both indications in Japan. Omalizumab is at the pre-registration stage for both indications in the US, New Zealand, Switzerland and Western Europe, and is currently registered for both indications in Australia.

L58 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L58 ANSWER 3 OF 23 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2002036168 EMBASE Anti-IgE-**antibodies** in the **treatment** of allergic diseases. Soler M.. M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 (45-49) 2002.
Refs: 25.
ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The humanized monoclonal Anti-IgE **antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This **treatment**, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic **asthma**, preventing exacerbations and reducing the need for inhaled and/or systemic steroid **treatment**. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new **treatment** may have an important place in the future **treatment** of moderate to severe allergic **asthma**, especially if the patient needs a complex **treatment** that still allows for recurrent exacerbations. A major advantage of this

treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L58 ANSWER 4 OF 23 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2002144694 EMBASE Immunoglobulin-E and anti-IgE **treatment** in lung disease. Chitkara R.K.; Sarinas P.S.A.; Fick Jr. R.B.. Dr. R.B. Fick Jr., DNAX Research, Inc., 901 California Avenue, Palo Alto, CA 94304, United States. robert.fick@dnax.org. Monaldi Archives for Chest Disease 56/6 (514-520) 2001.
Refs: 50.
ISSN: 1122-0643. CODEN: MACDEL. Pub. Country: Italy. Language: English. Summary Language: English.
AB A highly specific monoclonal **antibody** binding IgE (anti-IgE/omalizumab) has made it possible to determine the immunopathogenetic role that this reaginic **antibody** plays in human allergic disease. It is clear from recently completed studies that IgE is essential to the full generation of early and late asthmatic responses in human bronchoprovocation trials. Importantly, anti-IgE **treatment** of severe **asthma** disease significantly improves symptoms and reduces exacerbation episodes. Elevated serum levels of IgE are prominent in the clinical presentation of allergic bronchopulmonary mycoses and IgE-mediated Type I hypersensitivity reactions are of fundamental importance to the immunopathogenesis of allergic bronchopulmonary aspergillosis. Although the role of IgE in mediating immunity to helminth parasites is considerably less clear, it is safe to conclude that the overall balance of evidence does not support a primary role for IgE in host protection with regard to schistosomiasis and strongyloidiasis.

L58 ANSWER 5 OF 23 MEDLINE
2001262398 Document Number: 21203341. PubMed ID: 11307028. Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven R J; van Roomen C P; Thomas W R; de Boer M; Knol E F; Davis F M. (Tanox Pharma BV, Amsterdam, The Netherlands.. joostvanneerven@tanox.nl) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 400-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.
AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcepsilonRI on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether humanized anti-IgE mAb Hu-901 can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic **asthma** patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data clearly indicate that anti-IgE **antibodies** for the **treatment** of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE **treatment** on late-phase reactions noted in clinical studies. Copyright 2001 S. Karger AG, Basel

L58 ANSWER 6 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:186685 Document No.: PREV200200186685. Induction of apoptosis by IDEC-152 (anti-**CD23**) in lymphoma cells. Pathan, Nuzhat (1); Hariharan, Kandasamy (1); Hopkins, Michael; Saven, Alan; Reff, Mitchell (1); Hanna, Nabil (1); Grint, Paul (1). (1) IDEC Pharmaceuticals, San Diego, CA USA. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 367a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB IDEC-152 is a primatized monoclonal **antibody** to human **CD23**, the low-affinity receptor for IgE on B cells that has been implicated in the regulation of IgE synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses IgE synthesis. IDEC-152 is currently in clinical trials for use in allergic **asthma**. **CD23** is also expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a chimeric monoclonal **antibody** to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the **treatment** of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain **CD23** positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of apprx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong **antibody** dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of **CD23**, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L58 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2003 ACS
2000:535179 Document No. 133:149142 Production of tetravalent **antibodies**. Braslawsky, Gary Ronald; Hanna, Nabil; Hariharan, Kandasamy; Labarre, Michael J.; Huynh, Tri B. (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2000044788 A1 20000803, 65 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US1893 20000128. PRIORITY: US 1999-238741 19990128.

AB The present invention relates to a novel process for the prepn. of biol. active **antibody** dimers in a pharmaceutically acceptable compn. The homodimer may be anti-CD20 homodimer or anti-**CD23** homodimer. The dimers can be composed of two **antibody** mols. having the same antigen binding specificity and linked through a reducible, disulfide, or a non-reducible thioether, bond (homodimer). Alternatively, the dimers can be composed of two different **antibody** mols. having binding specificity for two distinct antigens (heterodimer). These dimers are useful for inducing hyper-crosslinking of membrane antigens. The present invention further relates to the use of biol. active **antibody**

dimers for the preferential killing or inhibition of selected cell populations in the **treatment** of diseases such as cancer, allergic disease or autoimmune disorders.

L58 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2003 ACS
2000:133697 Document No. 132:203144 Low-adenosine antisense oligonucleotide agents, compositions, kits and **treatments** for respiratory disorders. Nyce, Jonathan W. (East Carolina University, USA). PCT Int. Appl. WO 2000009525 A2 20000224, 1343 pp. DESIGNATED STATES: W: AU, CA, CN, MX, RU, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US17712 19990803. PRIORITY: US 1998-95212 19980803.

AB A compn. comprises a nucleic acid comprising an oligo antisense to a target such as polypeptide(s) assocd. with an ailment afflicting lung airways, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents. The agent of the invention may be prepd. by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more antisense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a universal base. The agent, compn. and formulations are used for prophylactic, preventive and therapeutic **treatment** of ailments assocd. with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasoconstriction, inflammation, allergies, **asthma**, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), ischemic conditions including ischemia itself, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, pancreatic cancer, lung cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastasis, etc., as well as all types of cancers with may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present **treatment** is suitable for administration in combination with other **treatments**, e.g. before, during and after other **treatments**, including radiation, chemotherapy, **antibody** therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The **treatment** of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs. The invention is exemplified with specificity and pharmacokinetic studies using phosphorothioated antisense oligonucleotides targeted to the adenosine receptors A1, A2a, A2b, and A3.

L58 ANSWER 9 OF 23 MEDLINE
2000177926 Document Number: 20177926. PubMed ID: 10712348. **CD23** exhibits negative regulatory effects on allergic sensitization and airway hyperresponsiveness. Haczku A; Takeda K; Hamelmann E; Loader J; Joetham A; Redai I; Irvin C G; Lee J J; Kikutani H; Conrad D; Gelfand E W. (Division of Basic Sciences, Department of Pediatrics, National Jewish Medical and Research Center, Denver, Colorado 80206, USA.) AMERICAN JOURNAL OF

RESPIRATORY AND CRITICAL CARE MEDICINE, (2000 Mar) 161 (3 Pt 1) 952-60. Journal code: 9421642. ISSN: 1073-449X. Pub. country: United States. Language: English.

AB The effects of an anti-**CD23** monoclonal **antibody** (B3B4) in **CD23**-deficient and **CD23**-overexpressing mice were compared in a murine model of allergic sensitization. After sensitization and challenge with OA, mice developed increased serum levels of OA-specific IgE and IgG(1) with airway eosinophilia and AHR when compared with nonsensitized animals. Anti-**CD23 treatment** was studied under two protocols: 10-d OA aerosol exposure and intraperitoneal sensitization followed by aerosol challenge. In both protocols anti-**CD23** significantly reduced IgE and IgG(1) levels, abolished eosinophilia, and normalized AHR in BALB/c and wild-type **CD23**+/+ mice but not in **CD23**-/- mice. These changes were associated with increases in IFN-gamma and decreases in IL-4 production, suggesting that **CD23** binding may affect not only IgE production but also the Th1/Th2 imbalance during the development of allergic AHR. Absence of **CD23** in gene-deficient mice significantly enhanced OA-specific IgE and IgG(1) levels, airway eosinophilia, and AHR when compared with **CD23**+/+ wild-type littermates after sensitization and airway challenge. Sensitized and challenged **CD23** transgenic mice also developed eosinophilic airway inflammation and methacholine hyperresponsiveness. However, the extent of AHR, BAL, and tissue eosinophilia in these animals showed a significant negative correlation with levels of **CD23** expression on splenic T and B cells, demonstrating a limiting role of **CD23** in the development of allergic AHR.

L58 ANSWER 10 OF 23 MEDLINE

1999438051 Document Number: 99438051. PubMed ID: 10508270. Critical role of **CD23** in allergen-induced bronchoconstriction in a murine model of allergic **asthma**. Dasic G; Juillard P; Graber P; Herren S; Angell T; Knowles R; Bonnefoy J Y; Kosco-Vilbois M H; Chvatchko Y. (Department of Immunology Geneva Biomedical Research Institute, Glaxo Wellcome Research and Development S.A., Geneva, Switzerland.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1999 Sep) 29 (9) 2957-67. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB **CD23**-deficient and anti-**CD23** monoclonal **antibody**-treated mice were used to investigate the role of the low-affinity receptor for IgE (**CD23**) in allergic airway inflammation and airway hyperresponsiveness (AHR). While there were no significant differences in ovalbumin (OVA)-specific IgE titers and tissue eosinophilia, evaluation of lung function demonstrated that **CD23** -/- mice showed an increased AHR to methacholine (MCh) when compared to wild-type mice but were completely resistant to the OVA challenge. Anti-**CD23** Fab fragment **treatment** of wild-type mice did not affect the MCh-induced AHR but significantly reduced the OVA-induced airway constriction. These results imply a novel role for **CD23** in lung inflammation and suggest that anti-**CD23** Fab fragment **treatment** may be of therapeutic use in allergic **asthma**.

L58 ANSWER 11 OF 23 SCISEARCH COPYRIGHT 2003 ISI (R)

1999:128094 The Genuine Article (R) Number: 163UJ. Cell lines of pulmonary and non-pulmonary origin as tools to study the effects of house dust mite proteinases on the regulation of epithelial permeability. Winton H L; Wan H; Cannell M B; Gruenert D C; Thompson P J; Garrod D R; Stewart G A; Robinson C (Reprint). ST GEORGE HOSP, SCH MED, DEPT PHARMACOL & CLIN PHARMACOL, CRANMER TERRACE, LONDON SW17 0RE, ENGLAND (Reprint); ST GEORGE HOSP, SCH MED, DEPT PHARMACOL & CLIN PHARMACOL, LONDON SW17 0RE, ENGLAND; UNIV CALIF SAN FRANCISCO, CARDIOVASC RES INST, UCSF GENE THERAPY CORE CTR, DEPT LAB MED, SAN FRANCISCO, CA 94143; UNIV CALIF SAN FRANCISCO, CARDIOVASC RES INST, UCSF GENE THERAPY CORE CTR, DEPT STOMATOL, SAN

FRANCISCO, CA 94143; UNIV WESTERN AUSTRALIA, QUEEN ELIZABETH II MED CTR, DEPT MED, PERTH, WA 6009, AUSTRALIA; UNIV MANCHESTER, SCH BIOL SCI, MANCHESTER, LANCS, ENGLAND; UNIV WESTERN AUSTRALIA, QUEEN ELIZABETH II MED CTR, DEPT MICROBIOL, PERTH, WA 6009, AUSTRALIA. CLINICAL AND EXPERIMENTAL ALLERGY (OCT 1998) Vol. 28, No. 10, pp. 1273-1285. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0954-7894. Pub. country: ENGLAND; USA; AUSTRALIA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background Allergenic and non-allergenic proteinases from house dust mites (HDM) cause loss of adhesion between airway epithelial cells that may result in a loss of functional cohesion between the cells and thus assist in allergen presentation. Improved cellular assay systems are needed to ascertain the mechanisms involved.

Objectives To survey a series of epithelial cell lines (Calu-3, 16HBE14o(-), NCI-H292 and A549 from human airways, and MDCK from dog kidney) and establish their utility for studies of the effects of HDM proteinases from D. pteronyssinus on epithelial permeability, To develop an improved method for measuring changes in epithelial permeability induced by HDM proteinases and other provocants.

Methods The permeability of epithelial monolayer cultures to mannitol was calculated from measurements of clearance using a technique that permits mathematical estimation and reduction of non-cellular diffusional constraints. Permeability was studied under control conditions and after perturbation of monolayers with HDM proteinases (separated into serine- and cysteine-proteinase classes) or chelation of extracellular Ca2+. Fluorescent **antibody** staining was used to investigate whether the cells expressed tight junctions (staining of ZO-1), desmosomes (staining of desmoplakin) and zonulae adherentes (staining of E-cadherin).

Results The Calu-3 line was identified as an airway cell line that expressed functional light junctions, desmosomes and zonulae adherentes. Calu-3 monolayers exhibited a low clearance and permeability to mannitol, similar to that seen in the extensively characterized MDCK cell line. Clearance and permeability were significantly increased by **treatment** with either HDM proteinase fraction or by calcium chelation. 16HBE14o(-) cells also had a low permeability to mannitol under control conditions and expressed a similar repertoire of functional proteins from major intercellular junctions. In contrast, NCI-H292 and A549 cell lines were functionally deficient in tight junctions, although they did express desmosomes and zonulae adherentes to a greater extent. Epithelial permeability was found to be a more appropriate and sensitive index of epithelial perturbation than was tracer clearance.

Conclusion These results suggest that the Calu-3 and 16HBE14o(-) cell lines are useful tools in studying the mechanism of HDM proteinases on airway epithelial cell function. HDM proteinases of both cysteine and serine mechanistic classes were found to perturb epithelial adhesion and function.

L58 ANSWER 12 OF 23 MEDLINE

1998385766 Document Number: 98385766. PubMed ID: 9720812. Activation of B-lymphocytes during pollen season. Effect of immunotherapy. Hakansson L; Heinrich C; Rak S; Venge P. (Department of Clinical Laboratory Sciences, University Hospital, Uppsala, Sweden.) CLINICAL AND EXPERIMENTAL ALLERGY, (1998 Jul) 28 (7) 791-8. Journal code: 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: B-lymphocytes play an important part in the allergic reaction as producers of IgE **antibodies**. OBJECTIVE: To investigate the cell surface expression of the activation antigens **CD23**, CD40 and HLA-DR on B-lymphocytes in birch pollen allergic patients before and during birch pollen season and to study the effect of immunotherapy. METHODS: The study included 24 birch pollen allergic patients half of whom were treated with immunotherapy against birch pollen before the start of the season. Eleven of the 24 patients had **asthma**. Blood samples were taken and lung function was registered before the season

began and before the immunotherapy **treatment** in January to February and during the season in May. The relative number of B-lymphocytes (CD19+) of the lymphocyte population and the cell surface expression of **CD23**, CD40 and HLA-DR on B-lymphocytes was measured by the use of flow cytometry. RESULTS: In the control group of patients the relative number and concentration of B-lymphocytes, the cell surface expression of **CD23**, CD40 and HLA-DR on B cells, and the serum concentration of IgE increased during season compared with before season. In contrast, in the immunotherapy treated patients no changes in the number of B cells or cell surface expression of **CD23**, CD40 and HLA-DR were demonstrated. CONCLUSION: The elevated expression of **CD23**, CD40 and HLA-DR on B cells, combined with increased levels of IgE in allergic patients during season could be explained by the effect of cytokines produced by activated TH2 cells. A shift from TH2 to TH1 cells might be the mechanism after the absence of signs of B-cell activation in immunotherapy treated patients. The prevention of increased cell surface expression on B cells by immunotherapy may constitute a significant mechanism behind the beneficial effects of immunotherapy in the **treatment** of pollen atopy.

L58 ANSWER 13 OF 23 SCISEARCH COPYRIGHT 2003 ISI (R)

1998:315648 The Genuine Article (R) Number: ZH754. Control of IgE responses. V. Oral administration of a synthetic derivative of the inner bacterial cell wall (SDZ 280.636) to sensitized mice induces isotype specific suppression of peak hapten specific IgE **antibody** forming cell responses, serum IgE levels and immediate hypersensitivity responses.. Auci D L (Reprint); Kleiner G I; Chice S M; Athanassiades T J; Dukor P; Durkin H G. SUNY HLTH SCI CTR, DEPT PATHOL, BROOKLYN, NY 11203 (Reprint); SANDOZ GMBH, FORSCHUNGSINST, A-1235 VIENNA, AUSTRIA. IMMUNOLOGICAL INVESTIGATIONS (MAR 1998) Vol. 27, No. 1-2, pp. 105-120. Publisher: MARCEL DEKKER INC. 270 MADISON AVE, NEW YORK, NY 10016. ISSN: 0882-0139. Pub. country: USA; AUSTRIA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB SDZ 280.636, a nontoxic diacyl glycerol derivative of muramyl dipeptide (MDP), a component of the inner bacterial cell wall, which is suitable for use in man, suppressed hapten specific IgE **antibody** forming cell (AFC) responses in spleen, serum levels of hapten specific IgE and hapten specific immediate hypersensitivity (IH) responses in skin, when fed to mice at the peak of a hapten specific IgE AFC response. In addition, serum levels of IL-6 appeared increased while IFN gamma was decreased. To induce these IgE responses, BALB/c mice were injected i.p. with BPO-KLH (benzylpenicilloyl-keyhole limpet hemocyanin) (10 mu g) in aluminum hydroxide gel (alum) on days 0, 21 and 42. Mice were fed (gavage) with either MDP or SDZ 280.636 (1.0 or 10 mg/kg) on day 44, or on days 44, 46 and 48, and killed on days 46 or 50, Numbers of BPO specific AFC in spleen, and serum levels of BPO specific immunoglobulins (IgG1, IgE and IgA) were determined (ELISPOT assay, ELISA). In addition, BPO specific IH responses were measured in these animals. Mice were injected in the right pinna with BPO-BSA (0.1 mu g) and in the left pinna with an equal volume of saline (0.05 ml). At 2 hr, pinnae were measured using a micrometer caliper. We found that 1 feeding with either MDP or SDZ 280.636 abrogated IgE AFC responses and dramatically suppressed serum levels of IgE, both in isotype specific fashion, and suppressed IH responses (>50%). 3 feedings with sDZ 280.636 also abrogated IgE AFC responses and further decreased serum levels of IgE. In contrast to SDZ 280.636, 3 **treatments** with MDP had opposite effects in that IgE AFC responses and serum levels of IgE dramatically increased. A single **treatment** with SDZ 280.636 appeared to increase serum levels of IL-6 up to three fold, while IFN gamma levels decreased. Our data suggest that SDZ 280.636 may be useful in the therapeutic and prophylactic management of human atopic disease such as allergic rhinitis, **asthma**, and other atopic diseases.

L58 ANSWER 14 OF 23 MEDLINE
97276838 Document Number: 97276838. PubMed ID: 9130531. Demonstration of the therapeutic potential of non-anaphylactogenic anti-IgE **antibodies** in murine models of skin reaction, lung function and inflammation. Heusser C H; Wagner K; Bews J P; Coyle A; Bertrand C; Einsle K; Kips J; Eum S Y; Lefort J; Vargaftig B B. (Asthma Allergy Research Department, Ciba Geigy Ltd., Basel, Switzerland.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1997 May-Jul) 113 (1-3) 231-5. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Allergies and allergic **asthma** are believed to be mediated by allergen-specific IgE **antibodies**. We have investigated the therapeutic potential of inhibiting endogenous IgE by a non-anaphylactogenic anti-mouse IgE **antibody** 1-5 with respect to its effects on antigen-induced skin reaction, lung function changes and lung inflammation in mice. METHODS: Mice were immunized with benzylpenicillinoyl-KLH or ovalbumin, and antigen-mediated skin reaction, bronchoconstriction, bronchopulmonary hyperresponsiveness (BHR) and lung eosinophilic inflammation determined in anti-IgE 1-5-treated versus untreated animals. RESULTS: Application of anti-IgE 1-5 inhibited (by 90%) the serum IgE and, 3-4 days after onset of **treatment**, blocked the antigen-induced skin reaction. Furthermore, the **antibody** also inhibited (by 90%) the antigen-induced infiltration of eosinophils into the lung. This latter effect seems to be mediated by blocking the IgE-**CD23** interaction and indicates that lung eosinophilic inflammation also depends on IgE. Moreover, when applied to rats passively sensitized with mouse IgE, **antibody** 1-5 inhibited the antigen-induced bronchoconstriction. A similar effect could be seen in actively immunized mice, where **antibody** 1-5 was able to inhibit (by 70%) the ovalbumin-induced bronchoconstriction as well as BHR. CONCLUSIONS: In summary, non-anaphylactogenic anti-IgE **antibodies** can markedly inhibit IgE levels and IgE-mediated allergic reactions. Since bronchoconstriction, BHR and lung eosinophilic inflammation can be suppressed, such **antibodies** may be attractive principles for the **treatment** of allergic **asthma**.

L58 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L58 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl.

WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the **treatment** of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative **treatment** of mice against arthritis using monoclonal anti-**CD23 antibody**, **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L58 ANSWER 17 OF 23 MEDLINE

96261632 Document Number: 96261632. PubMed ID: 8666888. Central role of immunoglobulin (Ig) E in the induction of lung eosinophil infiltration and T helper 2 cell cytokine production: inhibition by a non-anaphylactogenic anti-IgE **antibody**. Coyle A J; Wagner K; Bertrand C; Tsuyuki S; Bews J; Heusser C. (Ciba-Geigy Ltd., Asthma and Allergy Research Department, Pharmaceutical Division, Basel Switzerland.) JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Apr 1) 183 (4) 1303-10. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Elevated levels of immunoglobulin (Ig) E are associated with bronchial **asthma**, a disease characterized by eosinophilic inflammation of the airways. Activation of antigen-specific T helper (Th) 2 cells in the lung with the subsequent release of interleukin (IL) 4 and IL-5 is believed to play an important role in the pathogenesis of this disease. In this study, we have used a non-anaphylactogenic anti-mouse-IgE **antibody** to investigate the relationship between IgE, airway eosinophil infiltration, and the production of Th2 cytokines. Immunization of mice with house dust mite antigen increased serum levels of IgE and IgG. Antigen challenge of immunized but not control mice induced an infiltration of eosinophils in the bronchoalveolar lavage associated with the production of IL-4 and IL-5 from lung purified Thy1.2+ cells activated through the CD3-T cell receptor complex. Administration of the anti-IgE monoclonal **antibody** (mAb) 6h before antigen challenge neutralized serum IgE but not IgG and inhibited the recruitment of eosinophils into the lungs and the production of IL-4 and IL-5 but not interferon gamma. Studies performed using an anti-**CD23** mAb, **CD23** deficient and mast cell deficient mice suggest that anti-IgE mAb suppresses eosinophil infiltration and Th2 cytokine production by inhibiting IgE-**CD23**-facilitated antigen presentation to T cells. Our results demonstrate that IgE-dependent mechanisms are important in the induction of a Th2 immune response and the subsequent infiltration of eosinophils into the airways. Neutralization of IgE, for example, non-anaphylactogenic anti-IgE mAbs may provide a novel therapeutic approach to the **treatment** of allergic airway disease.

L58 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2003 ACS

1996:253474 Document No. 124:286548 Central role of immunoglobulin (Ig) E in the induction of lung eosinophil infiltration and T helper 2 cell cytokine production: inhibition by a non-anaphylactogenic anti-IgE **antibody** . Coyle, Anthony J.; Wagner, Kathrin; Bertrand, Claude; Tsuyuki, Shogo; Bews, John; Heusser, Christoph (Asthma Allergy Res. Dep., Ciba-Geigy Ltd., Basel, CH-4002, Switz.). Journal of Experimental Medicine, 183(4), 1301-10 (English) 1996. CODEN: JEMEAV. ISSN: 0022-1007. Publisher:

Rockefeller University Press.

AB Elevated levels of IgE are assocd. with bronchial **asthma**, a disease characterized by eosinophilic inflammation of the airways. Activation of antigen-specific T helper (Th) 2 cells in the lung with the subsequent release of interleukin (IL) 4 and IL-5 is believed to play an important role in the pathogenesis of this disease. In this study, we have used a non-anaphylactogenic anti-mouse-IgE **antibody** to investigate the relationship between IgE, airway eosinophil infiltration, and the prodn. of Th2 cytokines. Immunization of mice with house dust mite antigen increased serum levels of IgE and IgG. Antigen challenge of immunized but not control mice induced an infiltration of eosinophils in the bronchoalveolar lavage assocd. with the prodn. of IL-4 and IL-5 from lung purified Thy1.2+ cells activated through the CD3 T cell receptor complex. Administration of the anti-IgE monoclonal **antibody** (mAb) 6 h before antigen challenge neutralized serum IgE but not IgG and inhibited the recruitment of eosinophils into the lungs and the prodn. of IL-4 and IL-5 but not interferon .gamma.. Studies performed using an anti-**CD23** mAb, **CD23** deficient and mast cell deficient mice suggest that anti-IgE mAb suppress eosinophil infiltration and Th2 cytokine prodn. by inhibiting IgE-**CD23**-facilitated antigen presentation to T cells. Our results demonstrate that IgE-dependent mechanisms are important in the induction of a Th2 immune response and the subsequent infiltration of eosinophils into the airways. Neutralization of IgE by, e.g., non-anaphylactogenic anti-IgE mAbs may provide a novel therapeutic approach to the **treatment** of allergic airway disease.

L58 ANSWER 19 OF 23 MEDLINE

97012414 Document Number: 97012414. PubMed ID: 8859229. Decrease in **CD23**+ B lymphocytes and clinical outcome in asthmatic patients receiving specific rush immunotherapy. Kljaic-Turkalj M; Cvoriscec B; Tudoric N; Stipic-Markovic A; Rabatic S; Trescec A; Gagro A; Dekaris D. (Department of Pulmonary Diseases and Clinical Immunology, General Hospital, Sveti Duh, Zagreb, Croatia.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1996 Oct) 111 (2) 188-94. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB Rush immunotherapy (RIT) has been documented as useful in the **treatment** of patients with allergic bronchial **asthma**. To investigate the mechanisms of its action, we studied changes in the serum levels of total IgE, allergen-specific IgE and IgG4, and expression of **CD23** on peripheral blood B cells in patients receiving RIT. Twenty patients with perennial bronchial **asthma** were evaluated before the beginning of RIT, as well as 6 weeks and 6 months later. Compared to pretreatment values, the level of Der-p-specific IgG4 and IgE significantly increased after 6 weeks and 6 months of RIT, while the total serum IgE remained unchanged. Furthermore, after 6 months of RIT, the percentage of **CD23**+B cells and its **CD23** receptor density significantly decreased. Since the symptom score improved and the need for medication decreased, we evaluated RIT as a useful procedure. After 6 months, 30% of patients did not have an **asthma** attack, with no medication in the last month, while 10% of them were **asthma** free for the last 3 months. No significant correlation between the clinical improvement, and in vitro changes was found. Furthermore, the observed in vitro changes were not significantly different in patients who responded with clinical improvement, compared to those with unchanged intensity of **asthma**. In conclusion, during specific RIT we found a significant increase in Der-p-specific IgE and IgG4 **antibodies**, as well as a moderate decrease in **CD23** + B cells and its **CD23** receptor density. These findings suggest a change in the lymphokine profile of patients receiving specific immunotherapy, and that the inhibition of IL-4-induced B cell stimulation may be hypothesized as the most important mechanism.

L58 ANSWER 20 OF 23 SCISEARCH COPYRIGHT 2003 ISI (R)
93:137161 The Genuine Article (R) Number: KP495. ATOPIC-DERMATITIS - CORRELATION OF PERIPHERAL-BLOOD T-CELL ACTIVATION, EOSINOPHILIA AND SERUM FACTORS WITH CLINICAL SEVERITY. WALKER C (Reprint); KAGI M K; INGOLD P; BRAUN P; BLASER K; BRUIJNZEELKOOMEN C A F M; WUTHRICH B. SWISS INST ALLERGY & ASTHMA RES, SIAF, OBERESTR 22, CH-7270 DAVOS, SWITZERLAND (Reprint); ZURCHER HOCHGEBIRGSKLIN, DAVOS, SWITZERLAND; UNIV HOSP ZURICH, DEPT DERMATOL, ALLERGY UNIT, CH-8091 ZURICH, SWITZERLAND. CLINICAL AND EXPERIMENTAL ALLERGY (FEB 1993) Vol. 23, No. 2, pp. 145-153. ISSN: 0954-7894. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In the first part of this study peripheral blood lymphocyte subpopulations, their activation state and various serum parameters were measured in extrinsic and intrinsic atopic dermatitis (AD) patients compared to normal individuals. Beside the characteristic eosinophilia, significantly increased numbers of CD4+ T cells with increased expression of IL-2 receptors (IL-2R) and HLA-DR were noted in the AD patients. In addition, extrinsic AD patients showed increased numbers of **CD23** + B cells and decreased numbers of CD16+ natural killer cells. Moreover, increased serum levels of eosinophil cationic protein (ECP) and soluble IL-2R as well as soluble factors that prolong survival of eosinophils in vitro could be demonstrated. In the second section of this study we determine how these blood immunological parameters relate to the clinical severity of the skin lesions of AD, by weekly analysis of 12 AD patients attending a high altitude clinic for 3 to 6 weeks. The patients were divided into two groups on the basis of **treatment** with topical steroids, but during the observation period a significant improvement in clinical status was observed in all AD patients independent of topical steroid therapy. A progressive decrease in eosinophil and activated T cell numbers, soluble IL-2R levels and serum eosinophil survival prolonging activity could be demonstrated, which closely correlated with the clinical severity of the AD.

L58 ANSWER 21 OF 23 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
93121689 EMBASE Document No.: 1993121689. [sCD23 and sIL-2R in allergic children receiving immunotherapy during 18 months]. SCD23 Y SIL-2R EN NINOS ALERGICOS RECIBIENDO INMUNOTERAPIA DURANTE DIECIOCHO MESES. Blanco Quiros A.; Garrote Adrados J.A.; Lapena Lopez De Armendia S.; Andion Dapena R.; Linares Lopez P.. Facultad de Medicina, Pediatria, Ramon y Cajal 5,47005 Valladolid, Spain. Revista Espanola de Alergologia e Inmunologia Clinica 8/1 (17-24) 1993.
ISSN: 0214-1477. CODEN: REACEN. Pub. Country: Spain. Language: Spanish. Summary Language: Spanish; English.

AB The variations on total IgE, serum soluble interleukin-2 receptor (sIL-2R) and low affinity IgE (sCD23) due to immunotherapy (IT) were studied. Twenty-four children allergic to pollen or dermatophagoides were included; 16 patients were treated with IT and 8 only received symptomatic therapy or environmental control measures. Blood samples were collected before starting the **treatment** and they were repeated in all cases 18 months afterwards. In patients not treated with IT there was an increase of IgE ($p < 0.05$) and a decrease of sCD23 (p:0.023), whereas in children who received IT there were no significant changes. A mild decrease of sIL-2R was produced in both groups, but it was not significant. Before starting IT, there was a correlation between IgE and sIL-2R (p:0.19) and a lesser one between IgE and sCD23 (p: 0.065) but it disappeared after 18 months' IT. The sCD23 levels decrease very much during childhood and the IT seems to diminish this trend. Larger and longer studies will be needed to assess whether IT increases the sCD23 levels and whether these molecules have any anti-allergic function blocking the circulant IgE **antibodies**; nevertheless children are not the more convenient patients for these assays, due to normal IgE increase and sCD23 decrease produced along the childhood. There was not any difference in the 3 studied factors, neither before nor after the IT. In spite of previous

hypotheses, sCD23 and sIL-2R do not seem very useful for monitoring the outcome of IT.

L58 ANSWER 22 OF 23 SCISEARCH COPYRIGHT 2003 ISI (R)
92:686147 The Genuine Article (R) Number: JY843. ANTIINFLAMMATORY EFFECTS OF NEDOCROMIL SODIUM - INHIBITION OF ALVEOLAR MACROPHAGE FUNCTION. BORISH L (Reprint); WILLIAMS J; JOHNSON S; MASCALI J J; MILLER R; ROSENWASSER L J. UNIV COLORADO, HLTH SCI CTR, NATL JEWISH CTR IMMUNOL & RESP MED, 1400 JACKSON ST, DENVER, CO, 80206 (Reprint); FISONS CORP, ROCHESTER, NY, 00000 . CLINICAL AND EXPERIMENTAL ALLERGY (NOV 1992) Vol. 22, No. 11, pp. 984-990. ISSN: 0954-7894. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The IgE-dependent activation of mononuclear phagocytic cells through their capacity to express low affinity IgE receptors (FcepsilonRII) has been proposed as a mechanism for the development of airways inflammation in allergic **asthma**. This FcepsilonRII expression leads to the IgE-dependent production of the potent pro-inflammatory cytokines IL-1beta and TNF-alpha. Expression by monocytes of FcepsilonRII is regulated by several cytokines including interleukin-4, gamma- and alpha-interferons, and granulocyte-macrophage and macrophage colony stimulating factors. An anti-inflammatory effect of nedocromil on monocytes has been proposed as a possible mechanism for its anti-**asthma** activity. We therefore investigated the capacity of nedocromil to modulate mononuclear phagocyte FcepsilonRII expression and cytokine production. We used an anti-FcepsilonRII **antibody** and flow cytometric analysis to assess the capacity of nedocromil to modulate cytokine-induced FcepsilonRII expression in normals and asthmatics. Monocytes, THP-1 monocyte leukaemia cells, and alveolar macrophages were exposed to varying concentrations of these cytokines for 48 hr at 37-degrees-C with or without the additional presence of nedocromil (1-10 mum) and the per cent of monocytes expressing FcepsilonRII was determined. No changes in FcepsilonRII expression were observed. Subsequently, we investigated the capacity of nedocromil to affect the capacity of IgE plus anti-IgE complexes, allergen, and LPS (16 hr/37-degrees-C) to stimulate IL-1beta and IL-6 production. No changes were observed when nedocromil was applied concomitant with the stimulus. However, pre-**treatment** (30 min) with nedocromil was associated with a 59.5 +/- 5.6% inhibition of IL-6 production stimulated by allergen and 34.5 +/- 5.1% by anti-IgE. In conclusion, nedocromil does not modulate mononuclear phagocytic cell FcepsilonRII expression but does suppress IgE-dependent cytokine production. This may represent an important anti-inflammatory action of nedocromil in the **treatment** of reactive obstructive airways disease.

L58 ANSWER 23 OF 23 MEDLINE
91223680 Document Number: 91223680. PubMed ID: 1673878. Fc epsilon receptor II/**CD23**-positive lymphocytes in atopic dermatitis. I. The proportion of Fc epsilon RII+ lymphocytes correlates with the extent of skin lesion. Takigawa M; Tamamori T; Horiguchi D; Sakamoto T; Yamada M; Yoshioka A; Toda K; Imamura S; Yodoi J. (Department of Dermatology, Hamamatsu University School of Medicine, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 May) 84 (2) 275-82. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Cells expressing Fc receptors for IgE (Fc epsilon RII) were identified in the peripheral blood from patients with atopic dermatitis and with eczematous dermatitis, and normal non-atopic subjects by using monoclonal **antibodies** to human lymphocyte Fc epsilon RII, and to lymphoid cell-surface antigens by immunofluorescence staining. Based on the extent of the dermatitis patients were classified as severe (greater than 50% skin surface involved), moderate (50-10%) and mild (less than 10%). Patients with severe and moderate atopic dermatitis had 5.9% and 5.7% Fc epsilon RII+ peripheral blood mononuclear cells (PBMC), respectively, that were significantly higher than percentages in mild atopic dermatitis

patients (2.6%), severe to moderate eczematous dermatitis patients (2.3%), mild eczematous dermatitis patients (2.2%) and normal individuals (1.7%)(0.05 greater than P). In severe and moderate atopic dermatitis patients, 10% of Fc epsilon RII+ PBMC were T cells that preferentially expressed CD8, and the remainder B cells and monocytes. Fc epsilon RII+ T cells comprised 1% of peripheral T cells, while half or more of peripheral B cells expressed Fc epsilon RII. In mild atopic dermatitis patients, eczematous dermatitis patients and normal subjects. Fc epsilon RII were expressed exclusively on 25-35% of peripheral B cells. Short-term **treatment** and long-term follow-up of atopic dermatitis patients revealed that changes in the skin condition were related closely to fluctuations in the proportion of Fc epsilon RII+ PBMC. Total serum IgE levels and atopic respiratory allergy did not influence the percentage of Fc epsilon RII+ PBMC. These findings suggest that the percentage of Fc epsilon RII+ PBMC reflects the extent of atopic dermatitis.

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L60 ANSWER 1 OF 15 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2003124852 EMBASE Technology evaluation: Omalizumab, Genentech/Novartis/Tanox. Lazaar A.L.. A.L. Lazaar, Univ. of PA Medical Center Pulmonary, Allergy and Critical Care Division, 421 Curie Boulevard, Philadelphia, PA 19104-6160, United States. alazaar@mail.med.upenn.edu. Current Opinion in Molecular Therapeutics 5/1 (81-89) 2003.
ISSN: 1464-8431. CODEN: CUOTFO. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB Genentech, Novartis and Tanox have co-developed Genentech's anti-IgE humanized monoclonal **antibody** omalizumab for the **treatment** of allergic **rhinitis** and asthma. The **antibody** is currently undergoing phase II clinical trials for allergic **rhinitis** in Canada and phase III clinical trials for both indications in Japan. Omalizumab is at the pre-registration stage for both indications in the US, New Zealand, Switzerland and Western Europe, and is currently registered for both indications in Australia.

L60 ANSWER 2 OF 15 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
2002036168 EMBASE Anti-IgE-**antibodies** in the **treatment** of allergic diseases. Soler M.. M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 (45-49) 2002.
Refs: 25.
ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.
AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The humanized monoclonal Anti-IgE **antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This **treatment**, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and

reducing the need for inhaled and/or systemic steroid **treatment**. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new **treatment** may have an important place in the future **treatment** of moderate to severe allergic asthma, especially if the patient needs a complex **treatment** that still allows for recurrent exacerbations. A major advantage of this **treatment** lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L60 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS
2000:535179 Document No. 133:149142 Production of tetravalent **antibodies**. Braslawsky, Gary Ronald; Hanna, Nabil; Hariharan, Kandasamy; Labarre, Michael J.; Huynh, Tri B. (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2000044788 A1 20000803, 65 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US1893 20000128. PRIORITY: US 1999-238741 19990128.

AB The present invention relates to a novel process for the prepn. of biol. active **antibody** dimers in a pharmaceutically acceptable compn. The homodimer may be anti-CD20 homodimer or anti-**CD23** homodimer. The dimers can be composed of two **antibody** mols. having the same antigen binding specificity and linked through a reducible, disulfide, or a non-reducible thioether, bond (homodimer). Alternatively, the dimers can be composed of two different **antibody** mols. having binding specificity for two distinct antigens (heterodimer). These dimers are useful for inducing hyper-crosslinking of membrane antigens. The present invention further relates to the use of biol. active **antibody** dimers for the preferential killing or inhibition of selected cell populations in the **treatment** of diseases such as cancer, allergic disease or autoimmune disorders.

L60 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L60 ANSWER 5 OF 15 SCISEARCH COPYRIGHT 2003 ISI (R)
1999:149983 The Genuine Article (R) Number: 166LH. Decrease of serum levels of soluble **CD23** during immunotherapy in patients with perennial

allergic **rhinitis**. Tanaka A; Ohashi Y (Reprint); Nakai Y. OSAKA CITY UNIV, SCH MED, DEPT OTOLARYNGOL, ABENO KU, 1-4-3 ASAHIMACHI, OSAKA 5458585, JAPAN (Reprint); OSAKA CITY UNIV, SCH MED, DEPT OTOLARYNGOL, ABENO KU, OSAKA 5458585, JAPAN. ANNALS OF OTOLOGY RHINOLOGY AND LARYNGOLOGY (FEB 1999) Vol. 108, No. 2, Part 1, pp. 193-200. Publisher: ANNALS PUBL CO. 4507 LACLEDE AVE, ST LOUIS, MO 63108. ISSN: 0003-4894. Pub. country: JAPAN. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB There is increasing in vitro evidence that soluble **CD23** (sCD23) is capable of potentiating the synthesis of human IgE and is likely involved in the expression of allergic diseases. Our study has aimed at investigating whether serum sCD23 is elevated in patients with perennial allergic **rhinitis** as compared to nonatopic controls, whether sCD23 in perennial allergic **rhinitis** fluctuates during the natural course in untreated patients, and whether sCD23 is decreased by immunotherapy. This study included 139 patients with perennial allergic **rhinitis** due to Dermatophagoides farinae who gave informed consent to participation. They were divided into 2 groups - an untreated group and an immunotherapy group - according to their **treatment** background. Thirty-one nonallergic, healthy volunteers were included to serve as controls. Symptom scores and serum concentrations of IgE specific to D farinae and sCD23 were examined twice in each patient: at enrollment (first evaluation) and on a variant time course after enrollment (second evaluation). Serum concentrations of sCD23 were measured by a sandwich enzyme-linked immunosorbent assay. The level of sCD23 in patients with perennial allergic **rhinitis** was significantly higher than that in nonatopic controls ($p < .0001$). The level of sCD23 in perennial allergic **rhinitis** was correlated with the level of specific IgE against D farinae. The sCD23 level did not fluctuate during the natural course for a span of 2.8 +/- 2.7 years in untreated patients ($p = .1337$), but was significantly decreased in patients who received immunotherapy for 2.7 +/- 2.2 years ($p < .0001$). The rate of decrease in sCD23 was significantly correlated with the rate of decrease in specific IEE ($rs = .523$, $p < .0001$) and symptom scores ($rs = .450$, $p < .0001$). In conclusion, the reduction in sCD23 during immunotherapy is probably related to the decrease in specific IEE and also plays a role in mediating its clinical effect.

L60 ANSWER 6 OF 15 MEDLINE

1999109926 Document Number: 99109926. PubMed ID: 9893928. Effects of azelastine on the level of serum interleukin-4 and soluble **CD23** antigen in the **treatment** of nasal allergy. Ito H; Nakamura Y; Takagi S; Sakai K. (Department of Otorhinolaryngology, Nagoya City University, Medical School, Japan.) ARZNEIMITTEL-FORSCHUNG, (1998 Dec) 48 (12) 1143-7. Journal code: 0372660. ISSN: 0004-4172. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Research findings and various published studies point to interleukin 4 (IL-4) and **CD23** antigen as instrumental in allergic reactions of allergy patients because these two substances are part of the main triggering mechanisms in cells producing IgE **antibodies**. In this study it was investigated whether the control of IL-4 and **CD23** levels result in a decrease of the severity of allergic reactions. It is well known that azelastine hydrochloride (AZ, CAS 79307-93-0) suppresses symptoms of nasal allergy. The antiallergic activity of this drug includes the suppression of IgE **antibody** production, antigen-**antibody** reactions, liberation of mediators and mediator antagonism. One report states that the cytokines IL-2, IL-3, and IL-4 were suppressed by AZ in cultured cells. There have been no reports regarding cytokines in clinical **treatment** using AZ. Therefore, the effects of AZ **treatment** on IL-4, soluble **CD23**, and RAST (radioallergosorbent test) levels in the sera of allergic **rhinitis** patients were studied. The results show that the levels of IL-4 and soluble **CD23** were significantly reduced by the administration of AZ over a 4-week period, especially in patients

with "excellent" or "good" efficacy of therapy.

L60 ANSWER 7 OF 15 SCISEARCH COPYRIGHT 2003 ISI (R)
1998:315648 The Genuine Article (R) Number: ZH754. Control of IgE responses. V. Oral administration of a synthetic derivative of the inner bacterial cell wall (SDZ 280.636) to sensitized mice induces isotype specific suppression of peak hapten specific IgE **antibody** forming cell responses, serum IgE levels and immediate hypersensitivity responses.. Auci D L (Reprint); Kleiner G I; Chice S M; Athanassiades T J; Dukor P; Durkin H G. SUNY HLTH SCI CTR, DEPT PATHOL, BROOKLYN, NY 11203 (Reprint); SANDOZ GMBH, FORSCHUNGSINST, A-1235 VIENNA, AUSTRIA. IMMUNOLOGICAL INVESTIGATIONS (MAR 1998) Vol. 27, No. 1-2, pp. 105-120. Publisher: MARCEL DEKKER INC. 270 MADISON AVE, NEW YORK, NY 10016. ISSN: 0882-0139. Pub. country: USA; AUSTRIA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB SDZ 280.636, a nontoxic diacyl glycerol derivative of muramyl dipeptide (MDP), a component of the inner bacterial cell wall, which is suitable for use in man, suppressed hapten specific IgE **antibody** forming cell (AFC) responses in spleen, serum levels of hapten specific IgE and hapten specific immediate hypersensitivity (IH) responses in skin, when fed to mice at the peak of a hapten specific IgE AFC response. In addition, serum levels of IL-6 appeared increased while IFN gamma was decreased. To induce these IgE responses, BALB/c mice were injected i.p. with BPO-KLH (benzylpenicilloyl-keyhole limpet hemocyanin) (10 mu g) in aluminum hydroxide gel (alum) on days 0, 21 and 42. Mice were fed (gavage) with either MDP or SDZ 280.636 (1.0 or 10 mg/kg) on day 44, or on days 44, 46 and 48, and killed on days 46 or 50, Numbers of BPO specific AFC in spleen, and serum levels of BPO specific immunoglobulins (IgG1, IgE and IgA) were determined (ELISPOT assay, ELISA). In addition, BPO specific IH responses were measured in these animals. Mice were injected in the right pinna with BPO-BSA (0.1 mu g) and in the left pinna with an equal volume of saline (0.05 mi). At 2 hr, pinnae were measured using a micrometer caliper. We found that 1 feeding with either MDP or SDZ 280.636 abrogated IgE AFC responses and dramatically suppressed serum levels of IgE, both in isotype specific fashion, and suppressed IH responses (>50%). 3 feedings with sDZ 280.636 also abrogated IgE AFC responses and further decreased serum levels of IgE. In contrast to SDZ 280.636, 3 **treatments** with MDP had opposite effects in that IgE AFC responses and serum levels of IgE dramatically increased. A single **treatment** with SDZ 280.636 appeared to increase serum levels of IL-6 up to three fold, while IFN gamma levels decreased. Our data suggest that SDZ 280.636 may be useful in the therapeutic and prophylactic management of human atopic disease such as allergic **rhinitis**, asthma, and other atopic diseases.

L60 ANSWER 8 OF 15 MEDLINE
1998049156 Document Number: 98049156. PubMed ID: 9389288. An intranasal glucocorticoid inhibits the increase of specific IgE initiated during birch pollen season. Pullerits T; Praks L; Sjostrand M; Rak S; Skoogh B E; Lotvall J. (Department of Clinical Pharmacology, Goteborg University, Gothenburg, Sweden.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1997 Nov) 100 (5) 601-5. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB BACKGROUND: Recent in vitro findings show that glucocorticoids in combination with IL-4 can induce the synthesis of IgE, indicating that glucocorticoids may promote allergy. OBJECTIVE: A double-blind, placebo-controlled study was performed to evaluate the effect of an intranasal glucocorticoid on the levels of birch pollen-specific IgE **antibodies** in serum from patients with allergic **rhinitis** . METHODS: Eighteen patients with allergic **rhinitis** received **treatment** with an intranasal glucocorticoid (beclomethasone dipropionate, 400 microg/day) or placebo for 5 weeks, starting from the beginning of the birch pollen season. Blood samples for anti-birch IgE

evaluation were taken before **treatment** was initiated and at 2 and 5 weeks after the beginning of the study. RESULTS: The beclomethasone group (n = 9) had significantly lower symptom scores when compared with the placebo group (n = 9) (0.86 +/- 0.26 vs 2.79 +/- 0.76, p value = 0.01). Both the **treatment** group and the placebo group showed a trend of an increase in anti-birch IgE levels 2 weeks after the beginning of the **treatment** (from 33.1 +/- 13.1 kU/L to 44.9 +/- 20.9 kU/L in the beclomethasone group and from 53.2 +/- 18.9 kU/L to 64.1 +/- 22.1 kU/L in the placebo group). **Treatment** with beclomethasone returned anti-birch IgE levels to baseline by the end of the study, whereas in the placebo group the anti-birch IgE levels continued to increase (final values, 33.1 +/- 11.9 kU/L vs 72.6 +/- 23.2 kU/L, respectively). The change in IgE **antibody** levels in the placebo group was significantly higher than that in the beclomethasone group. No statistically significant changes in total IgE or soluble **CD23** levels were detected. CONCLUSION: We conclude that **treatment** with an intranasal glucocorticoid initiated at the beginning of the pollen season inhibits the induced increase in specific IgE.

L60 ANSWER 9 OF 15 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

97213377 EMBASE Document No.: 1997213377. Immunotherapy affects the seasonal increase in specific IgE and interleukin-4 in serum of patients with seasonal allergic **rhinitis**. Ohashi Y.; Nakai Y.; Kakinoki Y.; Ohno Y.; Tanaka A.; Masamoto T.; Sakamoto H.; Washio Y.; Kato A.. Dr. Y. Ohashi, Department of Otolaryngology, Osaka City University Medical School, 1-5-7 Asahimachi, Abeno, Osaka 545, Japan. Scandinavian Journal of Immunology 46/1 (67-77) 1997.

Refs: 28.

ISSN: 0300-9475. CODEN: SJIMAX. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB This study was designed to determine seasonal changes in cytokines, soluble **CD23** and specific IgE in the serum of patients with seasonal allergic **rhinitis**, and the effect of immunotherapy on these seasonal changes. Fifty- four patients with seasonal allergic **rhinitis** caused by Japanese cedar pollens were divided into a medication group and an immunotherapy group. The patients of the medication group were treated with nonsedating antihistamines alone during the pollen season. The patients of the immunotherapy group had been treated for variable periods (mean, 5.0 .+-. 3.2 years) with immunotherapy using Japanese cedar pollen antigens. Serum samples were collected before and during the pollen season from each patient, to determine specific IgE, interleukin-4 (IL-4), interferon-.gamma. (IFN-.gamma.) and soluble **CD23** levels in serum. A significant increase in specific IgE and IL-4 and a significant decrease in IFN-.gamma. were observed during the pollen season in the medication group. In contrast, in the immunotherapy group, none of specific IgE, IL-4 and IFN-.gamma. was significantly changed following natural exposure to pollens. However, these effects were not significant in patients undergoing immunotherapy for 3 or fewer years. Seasonal rates of increase in specific IgE and IL-4 differed significantly between good responders and poor responders to immunotherapy, but seasonal rates of decrease in IFN-.gamma. did not. A seasonal rate of increase in soluble **CD23** was significantly correlated with a seasonal rate of increase in specific IgE, in both the medication and the immunotherapy groups. The seasonal rate of increase in soluble **CD23** was significantly smaller in the good responders than in the poor responders to immunotherapy. In conclusion, pollen immunotherapy reduces the seasonal increase in specific IgE, IL-4 and soluble **CD23** in serum, and in addition switches the seasonal preferential activation of Th-2 cells to reciprocal activation of Th-1 cells with **treatment** over several years. It is likely that the mechanisms responsible for the clinically beneficial effects of immunotherapy principally involve the modulation of Th-2 rather than Th-1 cytokines.

L60 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS
1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L60 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS
1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the **treatment** of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative **treatment** of mice against arthritis using monoclonal anti-**CD23 antibody**, **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L60 ANSWER 12 OF 15 MEDLINE
97064730 Document Number: 97064730. PubMed ID: 8908280. Study on changes in the level of serum IL-4 and soluble CD 23(s-**CD23**) with immunotherapy in nasal allergy patients. Ito H; Suzuki M; Mamiya S; Takagi I; Baba S. (Department of Otorhinolaryngology, Nagoya City University Medical School, Japan.) ACTA OTO-LARYNGOLOGICA. SUPPLEMENT, (1996) 525 98-104. Journal code: 0370355. ISSN: 0365-5237. Pub. country: Norway. Language: English.

AB In type I allergy such as allergic **rhinitis**, not only immunocytes but also interleukin 4 (IL-4) and other cytokines are significant factors. In the present study we explored the course of change in IL-4 in the sera of allergic **rhinitis** patients upon immunotherapy. Assays of serum IL-4 were performed by the chemiluminescence sandwich enzyme immunoassay using AMPPD(3-(2'-spirodamantane)-4-methoxy-4-(3'-phophoryloxy+ ++) phenyl-1,2-dioxetane).

The results indicated that immunotherapy reduced the IL-4 level from the pre-**treatment** baseline but not significantly. However, as far as good responses to the therapy are concerned a significant decrease in IL-4 was seen, and s-**CD23**, assayed at the same time, was also significantly decreased by immunotherapy.

L60 ANSWER 13 OF 15 SCISEARCH COPYRIGHT 2003 ISI (R)
96:759058 The Genuine Article (R) Number: VL947. STUDY ON CHANGES IN THE LEVEL OF SERUM IL-4 AND SOLUBLE CD-23 (S-**CD23**) WITH IMMUNOTHERAPY IN NASAL ALLERGY PATIENTS. ITO H (Reprint); SUZUKI M; MAMIYA S; TAKAGI I; BABA S. NAGOYA CITY UNIV, SCH MED, DEPT OTORHINOLARYNGOL, MIZUHO KU, 1 KAWASUMI, MIZUHO CHO, NAGOYA, AICHI 467, JAPAN (Reprint). ACTA OTO-LARYNGOLOGICA (1996) Supp. 525, pp. 98-104. ISSN: 0001-6489. Pub. country: JAPAN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In type I allergy such as allergic **rhinitis**, not only immunocytes but also interleukin 4 (IL-4) and other cytokines are significant factors. In the present study we explored the course of change in IL-4 in the sera of allergic **rhinitis** patients upon immunotherapy. Assays of serum IL-4 were performed by the chemiluminescence sandwich enzyme immunoassay using AMPPD(3-(2'-spirodamantane)-4-methoxy-4-(3('')-phophoryloxy) phenyl-1,2-dioxetane). The results indicated that immunotherapy reduced the IL-4 level from the pre-**treatment** baseline but not significantly. However, as far as good responses to the therapy are concerned, a significant decrease in IL-4 was seen, and s-**CD23**, assayed at the same time, was also significantly decreased by immunotherapy.

L60 ANSWER 14 OF 15 MEDLINE
96086459 Document Number: 96086459. PubMed ID: 7582163. Platelet aggregation in IgE-mediated allergy with elevated soluble Fc epsilon RII/**CD23** level. Rogala B; Gumprecht J; Gawlik R; Strojek K. (Department and Clinic of Allergic and Internal Diseases, Silesian School of Medicine, Zabrze, Poland.) JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY, (1995 May-Jun) 5 (3) 161-5. Journal code: 9107858. ISSN: 1018-9068. Pub. country: Spain. Language: English.
AB In 25 house dust mite-sensitive patients with perennial allergic **rhinitis**, an analysis of platelet aggregation tests (dual-channel aggregometer, Chronolog Corp, 345 model) induced by adenosine diphosphate (ADP) was carried out. The levels of total serum IgE specific **antibodies** against Dermatophagoides pteronyssinus and the soluble form of the low affinity IgE receptor (sFc epsilon RII/sCD23) were estimated as well. The study was carried out in a dynamic state, before and after 2 years of **treatment** with specific immunotherapy. We observed a significantly diminished platelet aggregation response, which partially improved after **treatment**. The results of this study suggest that platelet hyporesponsiveness might be involved in the pathogenesis of house dust mite hypersensitivity.

L60 ANSWER 15 OF 15 MEDLINE
91223680 Document Number: 91223680. PubMed ID: 1673878. Fc epsilon receptor II/**CD23**-positive lymphocytes in atopic dermatitis. I. The proportion of Fc epsilon RII+ lymphocytes correlates with the extent of skin lesion. Takigawa M; Tamamori T; Horiguchi D; Sakamoto T; Yamada M; Yoshioka A; Toda K; Imamura S; Yodoi J. (Department of Dermatology, Hamamatsu University School of Medicine, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 May) 84 (2) 275-82. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Cells expressing Fc receptors for IgE (Fc epsilon RII) were identified in the peripheral blood from patients with atopic dermatitis and with eczematous dermatitis, and normal non-atopic subjects by using monoclonal **antibodies** to human lymphocyte Fc epsilon RII, and to lymphoid cell-surface antigens by immunofluorescence staining. Based on the extent

of the dermatitis patients were classified as severe (greater than 50% skin surface involved), moderate (50-10%) and mild (less than 10%). Patients with severe and moderate atopic dermatitis had 5.9% and 5.7% Fc epsilon RII+ peripheral blood mononuclear cells (PBMC), respectively, that were significantly higher than percentages in mild atopic dermatitis patients (2.6%), severe to moderate eczematous dermatitis patients (2.3%), mild eczematous dermatitis patients (2.2%) and normal individuals (1.7%)(0.05 greater than P). In severe and moderate atopic dermatitis patients, 10% of Fc epsilon RII+ PBMC were T cells that preferentially expressed CD8, and the remainder B cells and monocytes. Fc epsilon RII+ T cells comprised 1% of peripheral T cells, while half or more of peripheral B cells expressed Fc epsilon RII. In mild atopic dermatitis patients, eczematous dermatitis patients and normal subjects. Fc epsilon RII were expressed exclusively on 25-35% of peripheral B cells. Short-term **treatment** and long-term follow-up of atopic dermatitis patients revealed that changes in the skin condition were related closely to fluctuations in the proportion of Fc epsilon RII+ PBMC. Total serum IgE levels and atopic respiratory allergy did not influence the percentage of Fc epsilon RII+ PBMC. These findings suggest that the percentage of Fc epsilon RII+ PBMC reflects the extent of atopic dermatitis.

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L62 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
2002:220424 Document No. 136:246408 Combination therapy for **treatment** of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.
AB The present invention concerns **treatment** of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L62 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.
AB The authors disclose the prepn. and characterization of murine monoclonal

and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L62 ANSWER 3 OF 11 MEDLINE

1998202080 Document Number: 98202080. PubMed ID: 9543080. Changes in **CD23** expression of blood and skin in atopic **eczema** after Chinese herbal therapy. Banerjee P; Xu X J; Poulter L W; Rustin M H. (Department of Dermatology, Royal Free Hospital School of Medicine, London, UK.) CLINICAL AND EXPERIMENTAL ALLERGY, (1998 Mar) 28 (3) 306-14. Journal code: 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: Aberrant expression of **CD23** (low affinity IgE receptor) on cells of the monocyte/macrophage series in peripheral blood and lesional skin of patients with atopic **eczema** has been demonstrated. It is not known whether this abnormality results from a fundamental systemic problem of the monocytes of these patients or reflects local changes to cell populations within the skin tissues. OBJECTIVES: This study was designed to determine whether this aberrant expression was caused by local cutaneous influences on mature cells or fundamental changes in monocyte differentiation. The possible relationship between these aberrations and clinical severity was also investigated by repeating these immunopathological studies after a course of efficacious **treatment** with Chinese herbal therapy (CHT). METHODS: Peripheral blood mononuclear cells were obtained from patients with atopic **eczema** before, and after 8 weeks of **treatment**. Efficacy of CHT was quantified on clinical grounds. Monocytes were isolated by adherence to plastic and cultured for up to 7 days. Samples were harvested at 2, 5 and 7 days of culture and cytospins prepared. Immunocytochemical staining to identify phenotypic subsets was performed on the monocytes at time 0 and on maturing cells from culture. This immunocytology was quantified using computerized image analysis equipment to determine the emergence of macrophage subsets and their level of **CD23** expression. Biopsies were taken from lesional skin before and after **treatment** and immunohistology was performed on cryostat sections to determine the number of antigen presenting cells expressing **CD23** as well as the level of expression of these molecules. RESULTS: The results showed that increased numbers of monocytes from patients with atopic **eczema** express **CD23** at day 0 and that cultured monocytes from these patients differentiate faster during the 7 day culture period as compared to normal controls. Efficacious **treatment** did not affect the number of peripheral blood monocytes expressing **CD23**. However, **treatment** did lead to a significant decrease in the number of **CD23**+ mature macrophages in the skin as well as a reduction in the level of expression of this moiety. These results demonstrate that changes in clinical severity are more closely related to the expression of **CD23** on mature antigen presenting cells in lesional skin rather than to differentiating peripheral blood monocyte **CD23** expression. CONCLUSIONS: These results suggests that local factors within lesional skin govern the accumulation and the expression of **CD23** on mature macrophages and that these factors may be more relevant to the pathogenesis of the disease than aberrations in **CD23** expression that may occur systemically.

L62 ANSWER 4 OF 11 MEDLINE

97191337 Document Number: 97191337. PubMed ID: 9039295. Modulation by Chinese herbal therapy of immune mechanisms in the skin of patients with atopic **eczema**. Xu X J; Banerjee P; Rustin M H; Poulter L W.

(Department of Dermtology, Royal Free Hospital and School of Medicine, London, UK.) BRITISH JOURNAL OF DERMATOLOGY, (1997 Jan) 136 (1) 54-9. Journal code: 0004041. ISSN: 0007-0963. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Ten patients with atopic **eczema** (AE) received **treatment** with Chinese herbal therapy (CHT; Zemaphyte) for 2 months. The severity of the **eczema** was recorded and skin biopsies were taken from lesional (L) and non-lesional (NL) skin before and after **treatment** . The skin biopsies were stained to detect T-cell subsets (CD4, CD8, CD45Ro and CD25), macrophage subsets (RFD7), dendritic cells (RFD1). Langerhans cells (CD1), HLA-DR, low-affinity IgE receptors (**CD23**) and high-affinity IgE receptors (15A5, 22H7). A quantitative assessment of the numbers of positively stained cells was made. Monoclonal **antibody** binding specifically to **CD23**(Fc epsilon RII) was used, in combination with cell subset monoclonal **antibodies** to quantify the cellular distribution of **CD23** antigen in the skin. Following 2 months of **treatment** with CHT, erythema was reduced by 53%. There was also a significant reduction in HLA-DR expression. The numbers of RFD1 + **CD23** +, RFD7 + **CD23** +, CD1 + **CD23**+ and CD25 + cells in lesional skin decreased significantly after **treatment** (RFD1 + **CD23** + from 0.39 to 0.21, RFD7 + **CD23** + from 0.29 to 0.16. CD1 + **CD23** + from 0.24 to 0.09, CD25 + from 0.84 to 0.31 in epidermis and from 1.62 to 0.94 in dermis (mean cells numbers per unit area). No significant change in cell numbers in NL skin or expression of Fc epsilon RI in either L or NL samples was observed after **treatment**. This study confirms that CHT is clinically efficacious and that clinical improvement is associated with a significant reduction in antigen-presenting cells expressing **CD23**.

L62 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS

1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L62 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE,

SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the **treatment** of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative **treatment** of mice against arthritis using monoclonal anti-**CD23 antibody, CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L62 ANSWER 7 OF 11 MEDLINE

96184215 Document Number: 96184215. PubMed ID: 8620093. Association of immunological changes with clinical efficacy in atopic **eczema** patients treated with traditional Chinese herbal therapy (Zemaphyte). Latchman Y; Banerjee P; Poulter L W; Rustin M; Brostoff J. (Department of Immunology, UCL Medical School, London, UK.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1996 Mar) 109 (3) 243-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB The efficacy of the Chinese herbal therapy (Zemaphyte) has been well established as a **treatment** for atopic **eczema** (AE) in clinical trials. The purpose of this study was to probe the immunological changes that occurred when patients were treated with the herbs for a period of 8 weeks. This **treatment** decreased serum IgE complexes (p less than 0.05) but did not affect total serum IgE or **CD23** expression on peripheral blood monocytes. Peripheral blood mononuclear cells from patients before and after **treatment** were cultured overnight with interleukin 4 and the ability of this cytokine to induce **CD23** on monocytes from treated patients was found to be significantly diminished (p less than 0.01). Soluble interleukin 2 receptor and soluble vascular cell adhesion molecule were both raised in the serum of AE patients compared to control individuals. Both these parameters were decreased following **treatment** (p less than 0.05). All these changes coincided with improvement in erythema and surface damage scores. There was no alteration in soluble intracellular adhesion molecule or soluble **CD23**. The results of these investigations would suggest that this herbal **treatment** has the ability to target various immunological parameters which may be involved in the pathogenesis of AE.

L62 ANSWER 8 OF 11 SCISEARCH COPYRIGHT 2003 ISI (R)

95:786713 The Genuine Article (R) Number: TD446. PITYROSPORUM-OVALE EXTRACTS INCREASE INTERLEUKIN-4, INTERLEUKIN-LO AND IGE SYNTHESIS IN PATIENTS WITH ATOPIC **ECZEMA**. KROGER S; NEUBER K (Reprint); GRUSECK E; RING J; ABECK D. UNIV HAMBURG, HOSP EPPENDORF, DEPT DERMATOL & ALLERGOL, MARTINISTR 52, D-20246 HAMBURG, GERMANY (Reprint); UNIV HAMBURG, HOSP EPPENDORF, DEPT DERMATOL & ALLERGOL, D-20246 HAMBURG, GERMANY. ACTA DERMATO-VENEREOLOGICA (SEP 1995) Vol. 75, No. 5, pp. 357-360. ISSN: 0001-5555. Pub. country: GERMANY. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Evidence for a possible role of the lipophilic yeast Pityrosporum ovale in the pathophysiology of atopic **eczema** has been found both in laboratory and therapeutical studies. Positive type I prick test reactions to P. ovale correlate with the intensity of eczematous skin lesions in the head and neck regions of patients with atopic **eczema**, Furthermore, antifungal **treatment** has been shown to be helpful in atopic **eczema**, In the present study the effect of P. ovale on IgE synthesis and cytokine production (IL-2, IFN gamma, IL-4, IL-10) was investigated in patients with atopic **eczema**, in vitro. Eight

patients with atopic **eczema** were studied; of these, 5 patients had specific IgE **antibodies** against P. ovale, as determined by fluoroimmunoassay (EAST). The control group consisted of 5 healthy non-atopic, P. ovale IgE-**antibody**-negative volunteers. Freshly isolated peripheral blood mononuclear cells (PBMC) were incubated in the presence of different antigen concentrations (0.01, 0.1, 1.0, 10 mu g/l x 10(6) cells) of P. ovale. IgE contents in the cell culture supematants were significantly elevated in RAST(+) patients with atopic **eczema** ($p<0.05$), compared with RAST(-) atopic **eczema** patients and healthy volunteers, Coincubation of P. ovale-stimulated PBMC with IL-4 (50 U/l/ 1x10(6) cells) resulted in a significantly higher IgE synthesis only in the RAST(+) atopic **eczema** patients, Additionally, incubation of PBMC from RAST(+) patients with atopic **eczema** led to an elevated synthesis of the T(H)2 related cytokines IL-4 and IL-10. Within the atopic **eczema** group, two subgroups differed markedly in their response to P. ovale antigen stimulation with a good correlation to the presence of specific IgE in serum and in vitro IL-4 and IL-10 production, The data support the assumption that P. ovale antigens might play a role in skin inflammation in at least a subgroup of patients with atopic **eczema** characterized by the presence of specific IgE **antibodies** to P. ovale.

L62 ANSWER 9 OF 11 SCISEARCH COPYRIGHT 2003 ISI (R)
93:137161 The Genuine Article (R) Number: KP495. ATOPIC-DERMATITIS - CORRELATION OF PERIPHERAL-BLOOD T-CELL ACTIVATION, EOSINOPHILIA AND SERUM FACTORS WITH CLINICAL SEVERITY. WALKER C (Reprint); KAGI M K; INGOLD P; BRAUN P; BLASER K; BRUIJNZEELKOOMEN C A F M; WUTHRICH B. SWISS INST ALLERGY & ASTHMA RES, SIAF, OBERESTR 22, CH-7270 DAVOS, SWITZERLAND (Reprint); ZURCHER HOCHGEBIRGSKLIN, DAVOS, SWITZERLAND; UNIV HOSP ZURICH, DEPT DERMATOL, ALLERGY UNIT, CH-8091 ZURICH, SWITZERLAND. CLINICAL AND EXPERIMENTAL ALLERGY (FEB 1993) Vol. 23, No. 2, pp. 145-153. ISSN: 0954-7894. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In the first part of this study peripheral blood lymphocyte subpopulations, their activation state and various serum parameters were measured in extrinsic and intrinsic atopic dermatitis (AD) patients compared to normal individuals. Beside the characteristic eosinophilia, significantly increased numbers of CD4+ T cells with increased expression of IL-2 receptors (IL-2R) and HLA-DR were noted in the AD patients. In addition, extrinsic AD patients showed increased numbers of **CD23** + B cells and decreased numbers of CD16+ natural killer cells. Moreover, increased serum levels of eosinophil cationic protein (ECP) and soluble IL-2R as well as soluble factors that prolong survival of eosinophils in vitro could be demonstrated. In the second section of this study we determine how these blood immunological parameters relate to the clinical severity of the skin lesions of AD, by weekly analysis of 12 AD patients attending a high altitude clinic for 3 to 6 weeks. The patients were divided into two groups on the basis of **treatment** with topical steroids, but during the observation period a significant improvement in clinical status was observed in all AD patients independent of topical steroid therapy. A progressive decrease in eosinophil and activated T cell numbers, soluble IL-2R levels and serum eosinophil survival prolonging activity could be demonstrated, which closely correlated with the clinical severity of the AD.

L62 ANSWER 10 OF 11 MEDLINE
91223680 Document Number: 91223680. PubMed ID: 1673878. Fc epsilon receptor II/**CD23**-positive lymphocytes in atopic dermatitis. I. The proportion of Fc epsilon RII+ lymphocytes correlates with the extent of skin lesion. Takigawa M; Tamamori T; Horiguchi D; Sakamoto T; Yamada M; Yoshioka A; Toda K; Imamura S; Yodoi J. (Department of Dermatology, Hamamatsu University School of Medicine, Japan.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1991 May) 84 (2) 275-82. Journal code: 0057202.

ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Cells expressing Fc receptors for IgE (Fc epsilon RII) were identified in the peripheral blood from patients with atopic dermatitis and with eczematous dermatitis, and normal non-atopic subjects by using monoclonal **antibodies** to human lymphocyte Fc epsilon RII, and to lymphoid cell-surface antigens by immunofluorescence staining. Based on the extent of the dermatitis patients were classified as severe (greater than 50% skin surface involved), moderate (50-10%) and mild (less than 10%). Patients with severe and moderate atopic dermatitis had 5.9% and 5.7% Fc epsilon RII+ peripheral blood mononuclear cells (PBMC), respectively, that were significantly higher than percentages in mild atopic dermatitis patients (2.6%), severe to moderate eczematous dermatitis patients (2.3%), mild eczematous dermatitis patients (2.2%) and normal individuals (1.7%)(0.05 greater than P). In severe and moderate atopic dermatitis patients, 10% of Fc epsilon RII+ PBMC were T cells that preferentially expressed CD8, and the remainder B cells and monocytes. Fc epsilon RII+ T cells comprised 1% of peripheral T cells, while half or more of peripheral B cells expressed Fc epsilon RII. In mild atopic dermatitis patients, eczematous dermatitis patients and normal subjects. Fc epsilon RII were expressed exclusively on 25-35% of peripheral B cells. Short-term **treatment** and long-term follow-up of atopic dermatitis patients revealed that changes in the skin condition were related closely to fluctuations in the proportion of Fc epsilon RII+ PBMC. Total serum IgE levels and atopic respiratory allergy did not influence the percentage of Fc epsilon RII+ PBMC. These findings suggest that the percentage of Fc epsilon RII+ PBMC reflects the extent of atopic dermatitis.

L62 ANSWER 11 OF 11 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

91353239 EMBASE Document No.: 1991353239. Itch and atopic dermatitis: Clinical and experimental studies. Wahlgren C.-F.. Department of Dermatology, Karolinska Hospital, Karolinska Institute,Stockholm, Sweden. Acta Dermato-Venereologica, Supplement -/165 (4-53) 1991. ISSN: 0365-8341. CODEN: AVSUAR. Pub. Country: Norway. Language: English. Summary Language: English.

AB The aims of the study were to develop and evaluate methods for quantitative measurement of itch, to investigate the perception of itch in patients with atopic dermatitis (AD), and to measure itch in such patients during **treatment** with H1-receptor antagonists or cyclosporin A, thereby exploring possible mechanisms in the pathogenesis of itch in AD. In a double-blind, randomized, placebo-controlled, cross-over study of 30 AD patients using a potent, topical, antipruritic corticosteroid, two methods for measuring itch both successfully detected the itch-relieving effect of the corticosteroid. The two methods comprised new portable data-loggers (Pain-Track) for continuous recording of itch, and conventional visual analogue scale (VAS) forms for retrospective recording. The main advantages of the Pain-Track method are possibilities for frequent sampling, surveillance of compliance, and analysis of a large amount of data. Induction and measurement of experimental histamine-induced itch were studied in 38 healthy subjects. It was shown that pruritic stimuli should be presented in a random order so as to avoid systematic errors in the perception of itch. Two rating scales, a seven-stepped non-verbal scale on a Pain-Track logger, and a 100-mm VAS on a potentiometer, were found valid for continuous recording of itch. The perception of experimental itch was studied in 32 AD patients and 32 healthy controls. The itch responses provoked by wool fibres were significantly stronger in AD patients than in controls, whereas the histamine-induced dose-response curves for itch did not differ significantly between the two groups, who discriminated equally well between weak and strong histamine stimuli. No increased skin mast cell releasability was shown in vivo to compound 48/80 in AD patients. Their itch responses to the different pruritic stimuli did not correlate with clinical itch intensity, **eczema** score or serum IgE-level. In a double-blind, randomized, placebo-controlled, cross-over study of 25 AD

patients, the effect on clinical itch of a sedative (clemastine) and of a non-sedative (terfenadine) antihistamine did not differ from that of placebo, although both drugs had a pronounced H1-receptor-antagonizing effect in the skin and clemastine was significantly sedative. These findings support the view that histamine is not the major pruritogen in AD, and that sedation is not necessarily associated with itch relief. In a double-blind, randomized, placebo-controlled, cross-over study of 10 AD patients, 10 days' **treatment** with cyclosporin A (CSA), 5 mg/kg/day, significantly reduced itch intensity, **eczema** score and the number of peripheral blood eosinophils. Relapses were seen within 2-30 days of completion of CSA therapy. In at least 50% of the patients, CSA reduced the number of CD3+, CD4+, HLA-DR+, IgE+, **CD23**+ (low-affinity Fc-IgE receptor+), intercellular adhesion molecule-1+, and EG2+ (activated eosinophils) cells in lesional skin. The changes of itch magnitude in the patients did not strictly parallel any specific change in the occurrence of these cell surface markers. The mechanism of action for the antipruritic effect of CSA remains unclear, but it is hypothesized that cytokines may be involved in the pathogenesis of itch in AD.

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=> s l28 and graft versus host
L63           0 L28 AND GRAFT VERSUS HOST

=> s l28 and GVH
L64           0 L28 AND GVH

=> s l28 and COPD
L65           1 L28 AND COPD

=> d 65 cbib abs
      1 ANSWERS ARE AVAILABLE.  SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):165
ANSWER NUMBERS NOT CORRECTLY SPECIFIED
Enter an answer number,        Example: 10
several answer numbers,        Example: 3,7,10
a range of answer numbers,     Example: 5-10
or a combination of these.     Example: 3,7,9-10,15
ENTER ANSWER NUMBER OR RANGE (1):d 165 1 cbib abs
ANSWER NUMBERS NOT CORRECTLY SPECIFIED
Enter an answer number,        Example: 10
several answer numbers,        Example: 3,7,10
a range of answer numbers,     Example: 5-10
or a combination of these.     Example: 3,7,9-10,15
ENTER ANSWER NUMBER OR RANGE (1):1

L65  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
2000:133697   Document No. 132:203144  Low-adenosine antisense oligonucleotide
     agents, compositions, kits and treatments for respiratory
     disorders.  Nyce, Jonathan W. (East Carolina University, USA).  PCT Int.
     Appl. WO 2000009525 A2 20000224, 1343 pp.  DESIGNATED STATES: W:  AU, CA,
     CN, MX, RU, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT,
     LU, MC, NL, PT, SE.  (English).  CODEN: PIXXD2.  APPLICATION: WO
     1999-US17712 19990803.  PRIORITY: US 1998-95212 19980803.
AB   A compn. comprises a nucleic acid comprising an oligo antisense to a
     target such as polypeptide(s) assocd. with an ailment afflicting lung
     airways, genes and mRNAs encoding them, genomic and mRNA flanking regions,
     intron and exon borders and all regulatory and functionally related
     segments of the genes and mRNAs encoding the polypeptides, their salts and
     mixts.  Various formulations contain a requisite carrier, and optionally
     other additives and biol. active agents.  The agent of the invention may
     be prepd. by selecting a target gene(s), genomic flanking region(s),
     RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s)
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afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more antisense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a universal base. The agent, compn. and formulations are used for prophylactic, preventive and therapeutic **treatment** of ailments assocd. with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (**COPD**), acute respiratory distress syndrome (ARDS), ischemic conditions including ischemia itself, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, pancreatic cancer, lung cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastasis, etc., as well as all types of cancers with may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present **treatment** is suitable for administration in combination with other **treatments**, e.g. before, during and after other **treatments**, including radiation, chemotherapy, **antibody** therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The **treatment** of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs. The invention is exemplified with specificity and pharmacokinetic studies using phosphorothioated antisense oligonucleotides targeted to the adenosine receptors A1, A2a, A2b, and A3.

=> d his

(FILE 'HOME' ENTERED AT 10:30:16 ON 23 APR 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:30:38 ON 23 APR 2003

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L1      2419928 S ANTIBODY
L2         3300 S L1 AND CD23
L3           90 S L2 AND CHIMERIC
L4            9 S L3 AND HUMANIZED
L5            9 DUP REMOVE L4 (0 DUPLICATES REMOVED)
L6            0 S L3 AND BINDING AFFINITY
L7            6 S L2 AND BINDING AFFINITY
L8            6 DUP REMOVE L7 (0 DUPLICATES REMOVED)
L9          218 S ANTIBODY BINDING AFFINITY
L10           0 S L9 AND ANTI-CD23
L11           0 S L9 AND CD23
L12           0 S L9 AND FC EPSILON RECEPTOR II
L13           0 S L9 AND "RSSKSLLYKDGKTYLN"
L14           0 S L9 AND "1X109 KA PER M"
L15           0 S L2 AND BIOCORE ASSAYS
L16           0 S L2 AND BIACORE ASSAY
L17         111 DUP REMOVE L9 (107 DUPLICATES REMOVED)
L18           0 S L17 AND CD23 ANTIBODY
L19          88 S L2 AND ANTAGONIST
L20          59 DUP REMOVE L19 (29 DUPLICATES REMOVED)
L21           0 S L2 AND "CLONE C11"
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L22           38 DUP REMOVE L3 (52 DUPLICATES REMOVED)
L23         1353 DUP REMOVE L2 (1947 DUPLICATES REMOVED)
L24           31 S L23 AND ARTHRITIS
L25           31 DUP REMOVE L24 (0 DUPLICATES REMOVED)
L26           25 S L23 AND LUPUS ERYTHEMATOSUS
L27           25 DUP REMOVE L26 (0 DUPLICATES REMOVED)
L28          192 S L23 AND TREATMENT
L29            8 S L28 AND ARTHRITIS
L30            8 DUP REMOVE L29 (0 DUPLICATES REMOVED)
L31            7 S L28 AND LUPUS ERYTHEMATOSUS
L32            7 DUP REMOVE L31 (0 DUPLICATES REMOVED)
L33            0 S L28 AND HASHIMOTOS THYROIDITIS
L34            5 S L28 AND MULTIPLE SCLEROSIS
L35            5 DUP REMOVE L34 (0 DUPLICATES REMOVED)
L36            3 S L28 AND DIABETES
L37            3 DUP REMOVE L36 (0 DUPLICATES REMOVED)
L38            4 S L28 AND UVEITIS
L39            4 DUP REMOVE L38 (0 DUPLICATES REMOVED)
L40           16 S L28 AND DERMATITIS
L41           16 DUP REMOVE L40 (0 DUPLICATES REMOVED)
L42            4 S L28 AND PSORIASIS
L43            4 DUP REMOVE L42 (0 DUPLICATES REMOVED)
L44            4 S L28 AND URTICARIA
L45            4 DUP REMOVE L44 (0 DUPLICATES REMOVED)
L46            3 S L28 AND NEPHROTIC SYNDROME
L47            3 DUP REMOVE L46 (0 DUPLICATES REMOVED)
L48            5 S L28 AND GLOMERULONEPHRITIS
L49            5 DUP REMOVE L48 (0 DUPLICATES REMOVED)
L50            0 S L28 AND INFLAMMATORY BOWEL DISEASE
L51            4 S L28 AND ULCERATIVE COLITIS
L52            4 DUP REMOVE L51 (0 DUPLICATES REMOVED)
L53            0 S L28 AND "CROHN'S DISASE"
L54            0 S L28 AND SJOGRENS SYNDROME
L55            3 S L28 AND ALLERGIES
L56            3 DUP REMOVE L55 (0 DUPLICATES REMOVED)
L57           23 S L28 AND ASTHMA
L58           23 DUP REMOVE L57 (0 DUPLICATES REMOVED)
L59           15 S L28 AND RHINITIS
L60           15 DUP REMOVE L59 (0 DUPLICATES REMOVED)
L61           11 S L28 AND ECZEMA
L62           11 DUP REMOVE L61 (0 DUPLICATES REMOVED)
L63            0 S L28 AND GRAFT VERSUS HOST
L64            0 S L28 AND GVH
L65            1 S L28 AND COPD

=> s l28 and insulitis
L66            3 L28 AND INSULITIS

=> dup remove l66
PROCESSING COMPLETED FOR L66
L67            3 DUP REMOVE L66 (0 DUPLICATES REMOVED)

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L67  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2003 ACS
1999:736930   Document No. 131:350265  Antibodies to CD23.
     Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan
     Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK).
     PCT Int. Appl. WO 9958679 A1 19991118, 81 pp.  DESIGNATED STATES: W:  AE,
     AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE,
     ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
     KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
     RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,
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ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L67 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the **treatment** of inflammatory, autoimmune or allergic disease. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23** -liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L67 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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L69 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
2000:133697 Document No. 132:203144 Low-adenosine antisense oligonucleotide agents, compositions, kits and **treatments** for respiratory disorders. Nyce, Jonathan W. (East Carolina University, USA). PCT Int. Appl. WO 2000009525 A2 20000224, 1343 pp. DESIGNATED STATES: W: AU, CA, CN, MX, RU, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US17712 19990803. PRIORITY: US 1998-95212 19980803.

AB A compn. comprises a nucleic acid comprising an oligo antisense to a target such as polypeptide(s) assocd. with an ailment afflicting lung airways, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents. The agent of the invention may be prepd. by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more antisense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a universal base. The agent, compn. and formulations are used for prophylactic, preventive and therapeutic **treatment** of ailments assocd. with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic **bronchitis**, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), ischemic conditions including ischemia itself, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, pancreatic cancer, lung cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastasis, etc., as well as all types of cancers with may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present **treatment** is suitable for administration in combination with other **treatments**, e.g. before, during and after other **treatments**, including radiation, chemotherapy, **antibody** therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The **treatment** of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs. The invention is exemplified with specificity and pharmacokinetic studies using phosphorothioated antisense oligonucleotides targeted to the adenosine receptors A1, A2a, A2b, and A3.

L69 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 **Antibodies** to **CD23**.
Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan

Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and humanized **antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the **treatment** of autoimmune and inflammatory disorders.

L69 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

1996:380154 Document No. 125:56235 Binding agents for **treatment** of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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L69 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

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to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

=> s l28 and type I diabetes
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L72 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
2002:594705 Document No. 137:139366 Immunoregulatory **antibodies** and uses thereof. Hariharan, Kandasamy; Hanna, Nabil (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002060485 A2 20020808, 103 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2621 20020131. PRIORITY: US 2001-772938 20010131; US 2001-855717 20010516; US 2001-985646 20011105; US 2001-PV331187 20011109.
AB A combination **antibody** therapy for treating **B cell malignancies** using an immunoregulatory **antibody**, esp. an anti-B7, anti-**CD23**, or anti-CD40L **antibody**, and a B-cell depleting **antibody**, esp. anti-CD19, anti-CD20, anti-CD22 or anti-CD37 **antibody**, is provided. Preferably, the combination therapy will comprise anti-B7 and anti-CD20 **antibody** administration. IDEC-131, IDEC-114, and Rituxan monoclonal **antibodies** are of special interest.

L72 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
2002:51297 Document No. 136:117380 **Treatment** of **B cell malignancies** using combination of B cell depleting **antibody** and immune modulating **antibody** related applications. Hanna, Nabil; Hariharan, Kandasamy (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2002004021 A1 20020117, 88 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US15677 20010516. PRIORITY: US 2000-PV217706 20000712; US 2001-772938 20010131.
AB A combination **antibody** therapy for treating **B cell malignancies** using an immunoregulatory **antibody**, esp. an anti-B7, anti-**CD23**, or anti-CD40L **antibody** and a B cell depleting **antibody**, esp. anti-CD19, anti-CD20, anti-CD22 or anti-CD37 **antibody** is

provided. Preferably, the combination therapy will comprise anti-B7 and anti-CD20 **antibody** administration.

L72 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:186685 Document No.: PREV200200186685. Induction of apoptosis by IDEC-152 (anti-**CD23**) in lymphoma cells. Pathan, Nuzhat (1); Hariharan, Kandasamy (1); Hopkins, Michael; Saven, Alan; Reff, Mitchell (1); Hanna, Nabil (1); Grint, Paul (1). (1) IDEC Pharmaceuticals, San Diego, CA USA. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 367a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB IDEC-152 is a primatized monoclonal **antibody** to human **CD23**, the low-affinity receptor for IgE on B cells that has been implicated in the regulation of IgE synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses IgE synthesis. IDEC-152 is currently in clinical trials for use in allergic asthma. **CD23** is also expressed at high levels in certain **B-cell malignancies**, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a chimeric monoclonal **antibody** to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the **treatment** of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain **CD23** positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of apprx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong **antibody** dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of **CD23**, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

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L76 ANSWER 1 OF 3 SCISEARCH COPYRIGHT 2003 ISI (R)
96:369839 The Genuine Article (R) Number: UJ686. THE EPSTEIN-BARR VIRUS-BINDING SITE ON CD21 IS INVOLVED IN **CD23** BINDING AND INTERLEUKIN-4-INDUCED IGE AND IGG4 PRODUCTION BY HUMAN B-CELLS. HENCHOZLECOANET S; JEANNIN P; AUBRY J P; GRABER P; BRADSHAW C G; POCHON S;

BONNEFOY J Y (Reprint). GLAXO INST MOLEC BIOL, DEPT IMMUNOL, 14 CHEMIN AULX, CASE POSTALE 674, 1228 PLAN OUATES, GENEVA, SWITZERLAND (Reprint); GLAXO INST MOLEC BIOL, DEPT IMMUNOL, GENEVA, SWITZERLAND. IMMUNOLOGY (MAY 1996) Vol. 88, No. 1, pp. 35-39. ISSN: 0019-2805. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human CD21 has previously been described as a receptor for the C3d,g and iC3b proteins of complement, as a receptor for the gp350/220 envelope glycoprotein of the Epstein-Barr virus (EBV) and also as a receptor for interferon-alpha (IFN-alpha). Structurally, CD21 consists of 15 to 16 short consensus repeats (SCR) of 60 to 75 amino acids followed by a transmembrane domain and an intracytoplasmic region. We reported that **CD23**, a low-affinity receptor for IgE (Fc epsilon R2), is a new functional ligand for CD21. We recently found that the sites of interaction of **CD23** on CD21 are on SCR 5 to 8 and 1-2. The first site is a lectin-sugar type of interaction and the second site is a protein-protein interaction. We report here that amongst the other ligands for CD21 (EBV, C3d,g and IFN-alpha), only EBV is able to inhibit the binding of **CD23** to CD21. Furthermore, even a peptide from gp350/220 of EBV known to bind to CD21 is able to decrease **CD23** binding to CD21. Since **CD23**/CD21 pairing is important in the control of IgE production, we tested the effect of the EBV-derived peptide on immunoglobulin production from peripheral blood mononuclear cells and purified tonsillar B cells. Interestingly, the EBV-peptide inhibited IgE and IgG4 production induced by interleukin-4, in a dose-dependent manner. The same results were obtained using either peripheral blood mononuclear cells or purified tonsillar B cells. Another CD21 ligand, C3, did not affect binding of **CD23** to CD21 nor the production of IgE and IgG4. This study indicates that **blocking CD23** binding to CD21 SCR 2 on human B cells selectively modulates immunoglobulin production.

L76 ANSWER 2 OF 3 MEDLINE

93318718 Document Number: 93318718. PubMed ID: 7687088. A study of the interrelationship between circulating IgG subclass anti-IgE autoantibodies, IgE and **soluble CD23** in asthma. Shakib F; Boulstridge L; Smith S J. (Department of Immunology, University Hospital, Queen's Medical Centre, Nottingham, U.K.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1993 Jan-Feb) 21 (1) 20-4. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB In this paper we hypothesise that circulating autoanti-IgE **antibodies**, which are found in allergic asthma patients, could potentially enhance IgE synthesis by **blocking** its binding to **CD23** on B lymphocytes, thereby potentiating the release of soluble fragments of **CD23** which have B cell growth-promoting activity. We have investigated this possibility indirectly by measuring soluble (s) **CD23** and IgG subclass anti-IgE **antibody** levels in asthmatic patients' sera, to find out if the two parameters are related. However, we were unable to show any significant correlations between serum IgG subclass anti-IgE activities and sCD23 levels. This may have been due, at least in part, to the heterogeneous epitope specificity of the autoanti-IgE being detected. Interestingly, there was a significant inverse correlation ($p = 0.0178$) between serum IgE and sCD23 levels in asthma; an observation which underlines the notion that binding of IgE to membrane **CD23** abrogates the release of sCD23. The present study confirms and extends previous reports of significantly raised circulating levels of IgG anti-IgE in asthma patients ($p = 0.0004$), by further demonstrating that IgG anti-IgE is mostly restricted to IgG1. Given that IgG1 binds very efficiently to C1q and Fc gamma Rs, our observation lends further support to the notion that IgG anti-IgE may facilitate the removal of IgE-allergen complexes by triggering IgG effector function pathways.

L76 ANSWER 3 OF 3 MEDLINE

93016851 Document Number: 93016851. PubMed ID: 1401061. Epidermal keratinocyte-derived basophil promoting activity. Role of interleukin 3 and **soluble CD23**. Dalloul A H; Arock M; Fourcade C; Beranger J Y; Jaffray P; Debre P; Mossalayi M D. (Laboratoire d'Immunologie, Centre National de la Recherche Scientifique URA625, CHU Pitie-Salpetriere, Paris, France.) JOURNAL OF CLINICAL INVESTIGATION, (1992 Oct) 90 (4) 1242-7. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Human epidermal keratinocytes (EK) secrete factors able to sustain the proliferation of early myeloid cells and, in particular, the generation of basophils. This activity was previously attributed to IL-3, although no definitive in situ demonstration of this cytokine was provided. In regard to the possible physiological relevance of these data, we investigated herein the nature of EK-derived factors responsible for basophil promotion. Our data show that EK-derived supernatants (EK-sup) contain IL-3 as well as **soluble CD23** (sCD23), both known for their colony stimulating activity. Messenger RNA for IL-3 and **CD23** were also detected in EK. **Blocking** experiments using specific neutralizing monoclonal **antibodies** (mAb) further indicate that EK-derived basophil promoting activity is mainly due to the presence of IL-3 and sCD23 in EK-sup. Furthermore, by contrast to IL-3, sCD23 secretion by EK is cortisone sensitive and highly enhanced by IL-4, suggesting distinct regulatory mechanisms for their production.

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L77 ANSWER 1 OF 49 MEDLINE
2002671484 Document Number: 22319404. PubMed ID: 12431394. Vaccination for birch pollen allergy. Induction of affinity-matured or **blocking** IgG **antibodies** does not account for the reduced binding of IgE to Bet v 1. Svenson Morten; Jacobi Henrik H; Bodtger Uffe; Poulsen Lars K; Rieneck Klaus; Bendtzen Klaus. (Institute for Inflammation Research, Rigshospitalet University Hospital, Blegdamsvej 9, Copenhagen DK-2100, Denmark.) MOLECULAR IMMUNOLOGY, (2003 Jan) 39 (10) 603-12. Journal code: 7905289. ISSN: 0161-5890. Pub. country: England: United Kingdom. Language: English.

AB Specific allergy vaccination (SAV) is associated with increased levels of allergen specific IgG in serum. It is not clear, however, to what extent qualitative changes in allergen binding to IgG may be induced as well. We therefore analyzed the binding of the major allergen in pollen of birch (Betula verrucosa) (Bet v 1), the major allergen in birch pollen, to serum IgG and IgE, separately and in competition. Sera from six birch pollen-allergic patients were obtained before and after 5 years of SAV, and binding was assessed with 125I-Bet v 1. Before SAV, IgG bound more than eight times the amount of Bet v 1 compared with IgE, and together they accounted for more than 85% of the serum binding capacity. While SAV induced minimal changes in IgE binding, the IgG binding capacities increased 6-32 times. In contrast, the binding avidities (K(d) 28-40pM) changed less than 20%, pre- and post-SAV IgG provided similar inhibition of Bet v 1 binding to IgE at equimolar levels, and cross inhibition studies between IgG and IgE showed low inter-individual differences. Following SAV, all sera reduced Bet v 1 binding to **CD23**(+) cells, correlating with reduced binding of Bet v 1 to IgE ($P<0.001$). These results show that high avidity IgG of low inter-individual difference in Bet v 1 binding quality is the dominant binding factor of Bet v 1 in sera of birch pollen-allergic patients, and that SAV-induced inhibition of binding of Bet v 1 to IgE can be explained mainly or solely by increased amounts of IgG.

L77 ANSWER 2 OF 49 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:370946 Document No.: PREV200200370946. **Antibodies** against the stalk region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239. http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.

AB The stalk region of human **CD23** comprising a.a. 48-153 was expressed in E. coli and purified. In addition a chimeric human **CD23** was prepared consisting of the extracellular region of **CD23** linked to a modified leucine zipper (LZ-**CD23**). Polyclonal antisera were produced in rabbits and shown to block binding of IgE to **CD23** both on cell surfaces as well as the interaction of LZ-**CD23** with IgE in an ELISA based assay. The antisera was also shown to inhibit IgE synthesis in an anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose dependent and essentially complete blockage of IgE production was seen at a relatively low dose of anti-stalk. FACS analysis using **CD23**+B lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal **antibodies** against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to **blocking** IgE production.

L77 ANSWER 3 OF 49 MEDLINE
2002663816 Document Number: 22311125. PubMed ID: 12423314. Necessity of the stalk region for immunoglobulin E interaction with **CD23**. Chen Bing-Hung; Ma Check; Caven Timothy H; Chan-Li Yee; Beavil Andrew; Beavil Rebecca; Gould Hannah; Conrad Daniel H. (Department of Microbiology and Immunology, Virginia Commonwealth University, Richmond, VA 23298, USA.) IMMUNOLOGY, (2002 Nov) 107 (3) 373-81. Journal code: 0374672. ISSN: 0019-2805. Pub. country: England: United Kingdom. Language: English.

AB Previously, a soluble mouse **CD23** chimera, composed of an N-terminal trimeric isoleucine zipper motif (lz) followed by the entire extracellular region (amino acids 48-331) of **CD23** (lz-CD2348-331), was prepared and exhibited strong binding to rodent immunoglobulin E (IgE). In the current study, we report the construction of a similar human chimeric protein (lz-huCD2345-321), as well as a series of murine chimeric lz-**CD23** mutants with incremental portions of stalk deleted, to further investigate the role of the stalk region in mediating the **CD23**-IgE interaction. All chimeric proteins were designed such that the predicted heptad structure of the stalk was retained. IgE binding, as determined by the capacity to inhibit 125I-IgE from binding to FcepsilonRI-bearing RBL-2H3 cells, and by surface plasmon-resonance analysis using an IgE-coated sensor chip, was unchanged from the original lz chimera and the binding parameters were similar to those of cell-surface **CD23**. The minimal murine chimera that retained IgE-binding activity was lz-CD23139-331, which still contains 35 amino acids of the stalk region. When the lz motif was linked to **CD23** amino acid 157 (or higher), significant IgE-binding capacity was lost. With human lz-**CD23**, as with mouse, deletion of the stalk greatly reduced IgE-binding ability. In summary, the data support the concept that at least a portion of the stalk region of **CD23** plays a crucial role in maintaining high-affinity/avidity interaction with IgE. The lz-**CD23** constructs represent a possible alternative for both **blocking** the IgE/FcepsilonRI interaction and inhibiting IgE production by B lymphocytes.

L77 ANSWER 4 OF 49 MEDLINE

2001212260 Document Number: 21103165. PubMed ID: 11160193. Murine B1 B cells require IL-5 for optimal T cell-dependent activation. Erickson L D; Foy T M; Waldschmidt T J. (Department of Pathology and Immunology Graduate Program, University of Iowa College of Medicine, Iowa City, IA 52242, USA.) JOURNAL OF IMMUNOLOGY, (2001 Feb 1) 166 (3) 1531-9. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB T helper cell-driven activation of murine B cells has been shown to depend upon CD40-CD40 ligand (CD40L) interactions and a defined set of cytokines. These observations are primarily based on the use of conventional B cells obtained from the spleen. Therefore, it is presently unclear whether all mature B cell subsets found in the mouse have an equal dependence upon CD40-CD40L interactions and use the same T cell-derived cytokines. The present study tested the response of splenic follicular and marginal zone as well as peritoneal B2 and B1 B cells to Th cell stimulation. Splenic and peritoneal B cell subsets were sort purified based on **CD23** expression, and cultured with rCD40L and cytokines or Th2 cells. The results demonstrate that follicular, marginal zone, and peritoneal B2 B cells require CD40-CD40L interactions and preferentially use IL-4 for optimal proliferation, differentiation, and isotype switching. In contrast, peritoneal B1 B cells use IL-5 in conjunction with CD40-CD40L interactions for maximal Th cell-dependent responses. Furthermore, B1 B cells are capable of proliferating, differentiating, and isotype switching in the absence of CD40-CD40L interactions. B1 B cells are able to respond to Th2 clones in the presence of anti-CD40L mAb as well as to Th2 clones derived from CD40L(-/-) mice. The CD40-CD40L-independent response of B1 B cells is attributable to the presence of both IL-4 and IL-5, and may explain the residual Ab response to T cell-dependent Ags in CD40L- or CD40-deficient mice, and in X-linked hyper-IgM (X-HIM) patients.

L77 ANSWER 5 OF 49 MEDLINE

2002012311 Document Number: 21302711. PubMed ID: 11409113. Mechanisms of **CD23** hyperexpression on B cells from patients with rheumatoid arthritis. De Miguel S; Galocha B; Jover J A; Banares A; Hernandez-Garcia C; Garcia-Asenjo J A; Fernandez-Gutierrez B. (Services of Rheumatology and Pathology, Hospital Clinico San Carlos, Madrid, Spain.) JOURNAL OF RHEUMATOLOGY, (2001 Jun) 28 (6) 1222-8. Journal code: 7501984. ISSN: 0315-162X. Pub. country: Canada. Language: English.

AB OBJECTIVE: To analyze the mechanisms involved in the characteristic hyperexpression of **CD23** on peripheral blood B cells from patients with rheumatoid arthritis (RA). METHODS: Peripheral blood mononuclear cells (PBMC) were obtained from patients with active disease and activated during 18 h with an anti-CD3 monoclonal **antibody** in the presence or absence of **blocking antibodies** to CD154 or CD40. PBMC were further purified by rosetting and **CD23** expression was assessed on B cells by flow cytometry after double staining (CD19/**CD23**). Lymphocytes were also isolated from synovial fluid (SF). CD154 expression was analyzed on PB or SF CD4+ T cells after double staining (CD4/CD154) by flow cytometry at basal conditions and after different stimuli [anti-CD3 or phorbol myristic acetate (PMA) plus ionomycin]. Co-culture experiments between SF and PB cells were performed to analyze the involvement of the CD40-CD154 interaction on **CD23** expression. CD154 and **CD23** expression was also analyzed on synovial membrane by immunohistochemical techniques. RESULTS: A high proportion of activated **CD23** B cells was detected in patients with RA. **Blocking** experiments with both anti-CD40 and anti-CD154 Mab showed a significant reduction in the proportion of PB B cells expressing **CD23**. Following activation with anti-CD3 Mab or PMA plus ionomycin, CD154 expression was mainly induced on PB CD4+ T cells. In co-culture experiments, SF T cells were more efficient than PB T cells in inducing CD40 dependent **CD23** expression on PB B cells. In addition, CD4+ T cells from synovial membrane clearly expressed CD154. CONCLUSION: Our results establish a link between CD154-CD40

pathway and **CD23** expression on PB B cells from patients with RA. T cells from the synovial microenvironment were active participants in this **CD23** expression, presumably in the context of cell recirculation.

L77 ANSWER 6 OF 49 MEDLINE

2001339631 Document Number: 21178645. PubMed ID: 11282013. Increased expression of **CD23** (Fc(epsilon) receptor II) by peripheral blood monocytes of aids patients. Miller L S; Atabai K; Nowakowski M; Chan A; Bluth M H; Minkoff H; Durkin H G. (Department of Pathology, State University of New York-Downstate Medical Center, Brooklyn, New York 11203, USA.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (2001 Mar 20) 17 (5) 443-52. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Monocytes expressing the Fcepsilon receptor II (**CD23**) play important roles in inflammatory and allergic immune responses. We found that peripheral blood monocytes of AIDS patients express increased levels of **CD23**, compared with monocytes of healthy HIV-1-seronegative individuals (controls) ($p < 0.05$). We compared expression of monocyte **CD23** with expression of monocyte Fcgamma receptors (CD16, CD32, CD64), plasma/serum levels of IgE (also IgM, IgG, IgA), and Th1 (IFN-gamma) and Th2 (IL-4, IL-10) cytokines. We found that monocyte **CD23** expression directly correlated with monocyte CD16 expression ($p < 0.01$, $R = 0.58$), which was also increased in AIDS patients; there was no correlation with CD32 or CD64 or with soluble factors in plasma/serum (i.e., IgE, IL-4, IL-10, and IFN-gamma). Interestingly, despite the known ability of IL-10 to downregulate monocyte **CD23** expression, plasma IL-10 levels were increased in these AIDS patients compared with controls ($p < 0.05$). We thus evaluated the effect of AIDS and control plasma or rhIL-10 to regulate **CD23** expression by monocytes in cultures (24 hr) of healthy human cells +/- treatment with anti-IL-10R **blocking antibody**. We found that anti-IL-10R **blocking antibody** treatment had no effect on monocyte **CD23** expression in cultures containing AIDS plasma, but increased monocyte **CD23** expression in cultures containing control plasma ($p < 0.05$) or rhIL-10. In conclusion, the identification of increased monocyte **CD23** expression in AIDS patients may further characterize the aberrant activated phenotype of monocytes during the immunopathogenesis of HIV-1 disease. Further, monocyte **CD23** expression does not appear to be suppressed by the IL-10-enriched environment in AIDS.

L77 ANSWER 7 OF 49 MEDLINE

2001140719 Document Number: 21113743. PubMed ID: 11159001. Mechanism of cooperative effects of rhinovirus and atopic sensitization on airway responsiveness. Grunstein M M; Hakonarson H; Hodinka R L; Maskeri N; Kim C; Chuang S. (Divisions of Pulmonary Medicine and Allergy, Immunology, and Infectious Diseases, Joseph Stokes, Jr. Research Institute, Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, PA 19104, USA.. grunstein@email.chop.edu) . AMERICAN JOURNAL OF PHYSIOLOGY. LUNG CELLULAR AND MOLECULAR PHYSIOLOGY, (2001 Feb) 280 (2) L229-38. Journal code: 100901229. ISSN: 1040-0605. Pub. country: United States. Language: English.

AB To elucidate the mechanistic interplay between rhinovirus (RV) exposure and atopic sensitization in regulating airway smooth muscle (ASM) responsiveness, isolated rabbit ASM tissue and cultured human ASM cells were passively sensitized with sera from atopic asthmatic or nonatopic nonasthmatic (control) subjects in the absence and presence of inoculation with RV serotype 16. Relative to control subjects, atopic asthmatic serum-sensitized and RV-inoculated ASM exhibited significantly increased contractility to acetylcholine, impaired relaxation to isoproterenol, and enhanced release of the proinflammatory cytokine interleukin-1beta. These effects were potentiated in atopic asthmatic serum-sensitized ASM

concomitantly inoculated with RV and inhibited by pretreating the tissues with monoclonal **blocking antibodies** against intercellular adhesion molecule (ICAM)-1 (CD54), the host receptor for RV serotype 16, or lymphocyte function-associated antigen (LFA)-1 (CD11a/CD18), the endogenous counterreceptor for ICAM-1. Moreover, RV inoculation was found to potentiate the induction of mRNA and surface protein expression of FcepsilonRII (**CD23**), the low-affinity receptor for IgE, in atopic asthmatic serum-sensitized ASM. Collectively, these observations provide new evidence demonstrating that 1) RV exposure and atopic sensitization act cooperatively to potentiate induction of proasthmatic changes in ASM responsiveness in association with upregulated proinflammatory cytokine release and FcepsilonRII expression and 2) the effects of RV exposure and atopic sensitization are mediated by cooperative ICAM-1-coupled LFA-1 signaling in the ASM itself.

L77 ANSWER 8 OF 49 MEDLINE

2001219184 Document Number: 21205870. PubMed ID: 11309819. Monoclonal **antibody** FMC7 detects a conformational epitope on the CD20 molecule: evidence from phenotyping after rituxan therapy and transfectant cell analyses. Serke S; Schwaner I; Yordanova M; Szczepek A; Huhn D. (Department of Hematology and Oncology, Humboldt University, Berlin, Germany.. serke@charite.de) . CYTOMETRY, (2001 Apr 15) 46 (2) 98-104. Journal code: 8102328. ISSN: 0196-4763. Pub. country: United States. Language: English.

AB Numerous studies have reported that monoclonal **antibody** (mAb) FMC7 detects an antigen present on only a subset of circulating B lymphocytes. In particular, this mAb may distinguish typical B-cell chronic lymphocytic leukemia (FMC7 negative) from other types of B-cell non-Hodgkin lymphoma (B-NHL; FMC7 positive). We treated patients with B-NHL with Rituxan, a chimeric CD20 mAb, and observed abrogation of staining not only with prototype CD20 mAb B-1 but also with mAb FMC7. To investigate the relation between antigens CD20 and FMC7, we performed mutual **blocking** studies that showed mutual inhibition of FMC7 and CD20. In addition, FMC7 modulated **CD23** expression and confirmed the presence of mAb B-1 in B-lymphoblastoid cell lines CESS and JVM. Transient transfection of myeloid cell line K562 with plasmid containing CD20-encoding cDNA produced de novo expressions of CD20 and FMC7. Our data indicate that FMC7 binds to a particular conformation of the CD20 antigen, probably to a multimeric CD20 complex. We assume that FMC7 stains positively only when CD20 antigen is present in high densities and in the postulated multimeric complex formation.

L77 ANSWER 9 OF 49 CAPLUS COPYRIGHT 2003 ACS

2000:475785 Document No. 133:103725 Method of preventing immune and hypersensitivity reactions. Perdue, Mary H.; Yang, Ping-cCang; Berin, M. Cecilia (McMaster University, Can.). PCT Int. Appl. WO 2000040713 A1 20000713, 95 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-CA15 20000106. PRIORITY: US 1999-PV114867 19990106.

AB The present invention describes methods of modulating the immune system, and in particular allergic reactions, by **blocking** or interfering with the interaction between **CD23** receptors and IgE-antigen complexes. The methods described are directed to preventing immune hypersensitivity responses such as in food allergy or respiratory allergies.

L77 ANSWER 10 OF 49 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

2001:311682 Document No.: PREV200100311682. Monoclonal **antibody** FMC7 detects a conformational epitope on the CD20 molecule: Evidence from phenotyping after Rituxan therapy and transfectant cell analyses. Serke, Stefan (1); Schwaner, Ingo (1); Yordanova, Maya (1); Szczepek, Agnes; Huhn, Dieter (1). (1) Department Hematology and Oncology, Humboldt-University, Berlin Germany. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 160a. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology. ISSN: 0006-4971. Language: English. Summary Language: English.

AB Numerous studies have reported that monoclonal **antibody** (MoAb) FMC7 detects an antigen present on only a subset of B lymphocytes. The use of FMC7 has been suggested for discrimination of typical B-CLL (FMC7 negative) from the varieties of other leukemic phase B-NHL (FMC7 positive). During treatment of B-NHL patients with Rituxan, a chimeric anti-CD20 MoAb, we have observed not only abrogation of staining with prototype anti-CD20 MoAb B-1, but also of staining with MoAb FMC7. To further investigate the relationship between CD20 and FMC7 antigens we have performed mutual **blocking** studies. Those studies revealed a mutual inhibition of FMC7 and CD20 MoAbs. When tested on B cell lines CESS and JVM, MoAb FMC7 induced a modulation of **CD23**-expression to the extent as known, and confirmed herein, for MoAb B-1. Finally, upon transient transfection of myeloid cell-line K562 with CD20-encoding mammalian expression vector, de novo expression of both CD20 and FMC7 antigen was observed. Our data indicate that MoAb FMC7 binds to a particular conformation of CD20 antigen, probably to a multimeric CD20 complex. Our data implicate that MoAb FMC7 yields positive staining only when CD20 antigen is present at high density and in the postulated particular multimeric complex formation.

L77 ANSWER 11 OF 49 MEDLINE

1999384123 Document Number: 99384123. PubMed ID: 10453043. **Blocking antibodies** induced by specific allergy vaccination prevent the activation of CD4+ T cells by inhibiting serum-IgE-facilitated allergen presentation. van Neerven R J; Wikborg T; Lund G; Jacobsen B; Brinch-Nielsen A; Arnved J; Ipsen H. (ALK-Abello, Horsholm, Denmark; and Lung and Allergy Clinic, Copenhagen, Denmark.. joost-vanneerven@tanox.nl) . JOURNAL OF IMMUNOLOGY, (1999 Sep 1) 163 (5) 2944-52. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Allergen-specific CD4+ T lymphocytes are activated at extremely low allergen concentrations in vivo as a result of serum-facilitated allergen presentation (S-FAP). It is not clear at present if specific allergy vaccination (SAV) has an effect on this mechanism. Here we show that birch allergen-specific serum-IgE facilitates the presentation of Bet v 1, the major birch pollen allergen, to Bet v 1-specific CD4+ T lymphocytes by a factor of >100. This process is **CD23** mediated, could be detected in sera from the majority of birch-allergic patients, and was clearly dose dependent. S-FAP of Bet v 1 was inhibited in patients undergoing long-term birch SAV, but not by sera from patients undergoing grass SAV, indicating that birch-specific Abs are involved. This resulted in decreased proliferation and IL-4, IL-5, IL-10, and IFN-gamma production of Bet v 1-specific T cells. The inhibition was already noted after 3-9 mo of SAV and could not be solely explained by increased serum levels of birch-specific IgG4. When IgG- and IgA/IgM-containing fractions of long-term SAV sera were used to inhibit S-FAP, only IgG-containing fractions were shown to inhibit S-FAP. These results indicate that **blocking** IgG Abs induced by SAV inhibits the occurrence of S-FAP at very low allergen concentrations, resulting in significantly higher allergen threshold levels to obtain T cell proliferation and cytokine production and thus allergen-induced late-phase responses.

L77 ANSWER 12 OF 49 MEDLINE

1999354925 Document Number: 99354925. PubMed ID: 10427971. Diminished responses to IL-13 by human monocytes differentiated in vitro: role of the IL-13Ralpha1 chain and STAT6. Hart P H; Bonder C S; Balogh J; Dickensheets H L; Vazquez N; Davies K V; Finlay-Jones J J; Donnelly R P. (Department of Microbiology and Infectious Diseases, School of Medicine, Flinders University of South Australia, Adelaide, Australia.. prue.hart@flinders.edu.au) . EUROPEAN JOURNAL OF IMMUNOLOGY, (1999 Jul) 29 (7) 2087-97. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB The primary IL-13 receptor complex on human monocytes is believed to be a heterodimer comprised of the IL-4R alpha chain and the IL-2R gamma chain (gamma(c))-like molecule, IL-13R alpha1. mRNA levels for IL-13R alpha1, but not IL-4R alpha, were markedly decreased in in vitro monocyte-derived macrophages (MDMac), and with increasing time of monocytes in culture correlated with the loss of IL-13 regulation of lipopolysaccharide-induced TNF-alpha production. Analysis of cell lines Daudi and THP-1 that differentially express gamma(c) and IL-13R alpha1 showed that IL-13 can activate STAT6 in IL-13R alpha1-positive THP-1 cells but not in gamma(c)-positive, IL-13R alpha1-negative Daudi cells. IL-13 activation of STAT6 was reduced in MDMac which was associated with diminished IL-13-induced expression of **CD23** and MHC class II. However, with reduced IL-13R alpha1 expression and low nuclear STAT6 activity, some IL-13-induced responses were unaltered in magnitude in MDMac. In the absence of functional IL-13R alpha1 and gamma(c), IL-13 must signal through an alternative receptor complex on MDMac. Experiments with a **blocking antibody** to IL-4R alpha showed that this chain remains an essential component of the IL-13 receptor complex on MDMac.

L77 ANSWER 13 OF 49 MEDLINE

1999279845 Document Number: 99279845. PubMed ID: 10353405. Up-regulation of interleukin-4 and **CD23**/FcepsilonRII in minimal change nephrotic syndrome. Cho B S; Yoon S R; Jang J Y; Pyun K H; Lee C E. (Department of Pediatrics, College of Medicine, Kyung Hee University, Seoul, Korea.) PEDIATRIC NEPHROLOGY, (1999 Apr) 13 (3) 199-204. Journal code: 8708728. ISSN: 0931-041X. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Although the pathogenesis of childhood minimal change nephrotic syndrome (MCNS) has not been clearly defined, the current hypothesis favors an involvement of T cell dysfunction. The symptom onset and the relapse of MCNS are frequently associated with allergy and increased IgE levels in sera. Since a T cell-derived cytokine interleukin-4 (IL-4) plays a key role in the regulation of IgE production and allergic response, we investigated the role of IL-4 in the pathophysiology of MCNS. Using fluorescence-activated cell scanning we observed a significantly higher expression of **CD23**, the type II IgE receptor (FcepsilonRII), on fresh B cells from active MCNS patients (n=22) compared with age-matched healthy normal controls (n=12). The upregulation of **CD23** correlates with greater IL-4 activity in the culture supernatant of MCNS peripheral blood lymphocytes (PBLs) than normal PBLs stimulated by mitogens, as assessed by the **CD23**-inducing effect of the PBL supernatant on tonsillar B cells. Furthermore, Northern blot and reverse transcription-based polymerase chain reaction analysis have revealed significantly elevated levels of IL-4 mRNAs both in mitogen-stimulated and unstimulated MCNS PBLs, compared with healthy normals or disease controls with other renal disorders. Together these results strongly suggest that the upregulation of IL-4 in T cells may be part of the T cell dysfunction involved in MCNS.

L77 ANSWER 14 OF 49 MEDLINE

1999110801 Document Number: 99110801. PubMed ID: 9893200. IL-4 and IgE-anti-IgE modulation of 15(S)-hydroxyeicosatetraenoic acid release by mononuclear phagocytes. Profita M; Vignola A M; Mirabella A; Siena L; Sala A; Gjomarkaj M; Bousquet J; Bonsignore G. (Istituto di Fisiopatologia

Respiratoria, C.N.R., Palermo, Italy.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1999 Jan) 103 (1 Pt 1) 159-64. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: IL-4 modulates the synthesis of IgE, the expression of **CD23**, and the release of 15(S)-hydroxyeicosatetraenoic (15[S]-HETE). OBJECTIVE: We evaluated the release of 15(S)-HETE by IL-4-stimulated monocytes and verified whether the observed increase in 15(S)-HETE release after passive sensitization and anti-IgE challenge of IL-4-treated monocytes was secondary to an increased **CD23** expression. METHODS: Human monocytes were incubated for 24, 48, and 72 hours with IL-4 (10 ng/mL) with or without an IgE-anti-IgE stimulation. We evaluated **CD23** expression by immunocytochemistry and 15(S)-HETE release by HPLC and RIA. To prove that the increase in 15(S)-HETE release was due to the effect of IL-4 on **CD23**, we performed experiments with an anti-**CD23 blocking** mAb. RESULTS: **CD23** expression and 15(S)-HETE release were significantly increased by IL-4, reaching a peak after 72 hours ($P < .02$). After passive sensitization with human IgE and anti-IgE challenge, IL-4-stimulated monocytes released higher amounts of 15(S)-HETE than IL-4-unstimulated monocytes ($P < .02$). Pretreatment with the anti-human B-cell **CD23** MHM6 mAb caused a dose-dependent inhibition of 15(S)-HETE release. CONCLUSIONS: This study shows that immunologic challenge of IL-4-treated, passively sensitized monocytes results in a **CD23**-dependent additional increase of 15(S)-HETE release, indicating the presence of a synergistic effect of IL-4 on **CD23** expression and 15(S)-HETE production.

L77 ANSWER 15 OF 49 MEDLINE

1998226802 Document Number: 98226802. PubMed ID: 9560263. Autologously up-regulated Fc receptor expression and action in airway smooth muscle mediates its altered responsiveness in the atopic asthmatic sensitized state. Hakonarson H; Grunstein M M. (Division of Pulmonary Medicine, The Joseph Stokes, Jr., Research Institute, The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, 34th Street and Civic Center Boulevard, Philadelphia, PA 19104, USA.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Apr 28) 95 (9) 5257-62. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB To elucidate the role of IgE-dependent mechanisms in inducing altered airway responsiveness in the atopic asthmatic state, the expression and actions of Fc receptor activation were examined in isolated rabbit tracheal smooth muscle (TSM) tissue and cultured cells passively sensitized with sera from atopic asthmatic patients or nonatopic/nonasthmatic (control) subjects. Relative to control tissues, the atopic asthmatic-sensitized TSM exhibited significantly increased maximal isometric contractility to acetylcholine ($P < 0.01$) and attenuated maximal relaxation responses and sensitivity (i.e.,-log ED50) to isoproterenol ($P < 0.005$). These changes in agonist responsiveness in atopic sensitized TSM were ablated by pretreating the tissues with a **blocking** mAb to the low affinity receptor for IgE, FcepsilonRII (i.e., **CD23**) or by depleting the sensitizing serum of its immune complexes. Moreover, in complimentary experiments, exogenous administration of IgE immune complexes to naive TSM produced changes in agonist responsiveness that were qualitatively similar to those obtained in the atopic asthmatic-sensitized state. Extended studies further demonstrated that, in contrast to their respective controls, atopic asthmatic serum-sensitized human and rabbit TSM tissue and cultured cells exhibited markedly induced mRNA and cell surface expression of FcepsilonRII, whereas constitutive expression of the IgG receptor subtype, FcgammaRIII, was unaltered. Finally, the up-regulated mRNA expression of FcepsilonRII observed following exposure of TSM to atopic asthmatic serum or to exogenously administered IgE immune complexes was significantly inhibited by pretreating the tissues or cells with anti-**CD23**

mAb. Collectively, these observations provide evidence demonstrating that the altered agonist responsiveness in atopic asthmatic sensitized airway smooth muscle is largely attributed to IgE-mediated induction of the autologous expression and activation of FcepsilonRII receptors in the airway smooth muscle itself.

L77 ANSWER 16 OF 49 MEDLINE
1998307269 Document Number: 98307269. PubMed ID: 9645362. Alpha-1 antitrypsin up-regulates human B cell differentiation selectively into IgE- and IgG4- secreting cells. Jeannin P; Lecoanet-Henchoz S; Delneste Y; Gauchat J F; Bonnefoy J Y. (Geneva Biomedical Research Institute, Immunology Department, Glaxo Wellcome R&D SA, Switzerland.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1998 Jun) 28 (6) 1815-22. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Numerous allergens have proteolytic activities. It has been speculated that this property may contribute to their allergenicity. Therefore, we have evaluated the effect of different physiological protease inhibitors (PI) on the regulation of human IgE synthesis. Unexpectedly, the serine PI, alpha-1 antitrypsin, also called alpha-1 protease inhibitor (alpha1PI), induced a potent and selective dose-dependent increase of IgE and IgG4 production by human tonsillar B cells stimulated with the IgE and IgG4 switch factors, IL-4 and anti-CD40 mAb. The other serine PI tested were inefficient. Furthermore, this effect of alpha1PI was accompanied by an increase in (1) germ-line and mature sigma mRNA transcription, (2) proliferation and (3) membrane **CD23** and CD21 expression, while the expression of other molecules involved in the regulation of IgE synthesis was unchanged. Since **CD23**-CD21 pairing plays a crucial role in the up-regulation of IgE synthesis, we have tested whether **blocking** this interaction affected alpha1PI-increased IgE production. The neutralizing anti-**CD23** mAb, Mab 25, partly reversed the IgE increase caused by alpha1PI. Moreover, alpha1PI potentiation of IgE synthesis was prevented by elastase, a natural substrate of alpha1PI, thereby suggesting that alpha1PI may inhibit endogenous B cell enzyme(s) involved in the down-regulation of IgE synthesis. Alpha1PI also potentiated IgE and IgG4 production by IL-4-stimulated peripheral blood mononuclear cells but was not a switch factor for IgE and IgG4 as it was unable to replace IL-4 or anti-CD40 mAb in inducing IgE and IgG4 production. In conclusion, this study shows that alpha1PI acts as a potent co-stimulus for IgE and IgG4 synthesis and suggests that the equilibrium between protease/ protease inhibitor participates in the control of human IgE and IgG4 synthesis.

L77 ANSWER 17 OF 49 MEDLINE
1998246917 Document Number: 98246917. PubMed ID: 9585825. Novel approaches to immunotherapy: epitopes, determinants, activators, or modulators?. Berrens L. (CBF. Leti, SA, Madrid, Spain.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1998 Jan-Feb) 26 (1) 27-33. Ref: 11. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB The immunological mechanism through which immunotherapy (IT) acts is not certainly known. The participation of the so-called "**blocking antibodies**" has not been proved and how it intervenes in the regulation of the production of IgE is still to be cleared, as it affects the action of lymphocytes Th1 and Th2. Nowadays, IT is based in the concept that the allergic reaction is somehow an antigen (allergen)-**antibody** (reagin) reaction. The possible modifications of IT are also based on the possibility to interfere in the antigen-**antibody** interaction. It has been proved in vitro that aqueous extracts of some allergens produce the consumption of complement, by its usual via, in which the C1 component is involved, without the mediation of **antibodies**, generating anaphylotoxin C3a, which is a powerful releaser of histamine, as well as C3b, which participates in the regulation of the cellular immunitary system. The term atopen should

therefore be used when referring to the unspecific activation or adjuvant activity of antigenically different allergens, due to their common structural or functional characteristics. The term allergen should then be used when describing those structural traits of the carrier molecule, which preferently produces the induction, and possible recognition of IgE **antibodies**. The action atopen and allergen as separate characteristics of a same molecule could theoretically become important in the future of therapeutics. The receptor of membrane CD21 for C3b, in B cells is a link for lectine **CD23** of lymphocytes B, which has been identified with the low affinity receptor IgE (Fce RII-**CD23**). In summary, the basic defect in atopy may reside in a defect of the receptor portion of reagin for atopen, but not in IgE. This means that in the nearby future, this fact should be taken into account in the search of drugs which participate in this kind of activation of allergic reaction, trying to modify or modulate the low affinity receptor IgE or even the high affinity receptor IgE.

L77 ANSWER 18 OF 49 MEDLINE

97332638 Document Number: 97332638. PubMed ID: 9188449. CD86 (B7-2) on human B cells. A functional role in proliferation and selective differentiation into IgE- and IgG4-producing cells. Jeannin P; Delneste Y; Lecoanet-Henchoz S; Gauchat J F; Ellis J; Bonnefoy J Y. (Geneva Biomedical Research Institute, GlaxoWellcome Research and Development, Immunology Department, 14, Chemin des Aulx, CH-1228 Plan les Ouates, Geneva, Switzerland.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jun 20) 272 (25) 15613-9. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Immunoglobulin (Ig) E production by B cells requires two primary signals provided by T cells, interleukin (IL)-4 or IL-13 and CD40 ligand (CD40L). In addition, costimulatory signals, such as **CD23**-CD21 interaction, contribute further ensuring a selective control over this production. Recently, CD28, expressed on T cells, has been reported to be involved in this process. The CD28 ligands, CD80 (B7-1) and CD86 (B7-2), are expressed on human tonsillar B cells, and their expression is up-regulated by IL-4, IL-13, and/or an anti-CD40 monoclonal **antibody** (mAb). We have investigated whether signaling via the B7 molecules affects IgE synthesis. Human B cells were stimulated by IL-4 plus anti-CD40 mAb in the presence of different anti-B7 mAbs. Cross-linking of CD86 with IT2.2 potentiated IgE and IgG4 production and epsilon transcripts expression. The production of the other isotypes was not modulated. Conversely, the anti-CD80 and the other anti-CD86 mAbs tested had no effect. The increase of IgE and IgG4 production induced by IT2.2 was accompanied by an increase in proliferation, in cell surface density of **CD23**, and in **CD23** binding to CD21-expressing B cells. In contrast, the expression of other B cell surface molecules such as CD11a, CD30, and CD58 remained unaffected. Since IT2.2 favors **CD23**-CD21 pairing, we tested whether **blocking** this interaction affected IT2.2-increased IgE production. The neutralizing anti-**CD23** mAb, Mab 25, caused a dose-dependent inhibition of the effect of IT2.2 on IgE synthesis. Finally, IT2.2 potentiation on B cell proliferation and IgE production required the two primary signals, IL-4 and anti-CD40 mAb, since IT2.2 alone or in combination with only one of these stimuli did not show any effect on B cells. This study is the first demonstration of a signaling role for CD86. Together with IL-4 or IL-13 and CD40L, CD86 favors **CD23** -CD21 pairing and consequently functions as a selective and potent costimulus for human IgE and IgG4 synthesis.

L77 ANSWER 19 OF 49 MEDLINE

1998000978 Document Number: 98000978. PubMed ID: 9341771. Mouse **CD23** regulates monocyte activation through an interaction with the adhesion molecule CD11b/CD18. Lecoanet-Henchoz S; Plater-Zyberk C; Graber P; Gretener D; Aubry J P; Conrad D H; Bonnefoy J Y. (Geneva Biomedical

Research Institute, Glaxo Wellcome Research and Development, Switzerland.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Sep) 27 (9) 2290-4. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB **CD23** is expressed on a variety of hemopoietic cells. Recently, we have reported that **blocking CD23** interactions in a murine model of arthritis resulted in a marked improvement of disease severity. Here, we demonstrate that CD11b, the alpha chain of the beta 2 integrin adhesion molecule complex CD11b/CD18 expressed on monocytes interacts with **CD23**. Using a recombinant fusion protein (ZZ-**CD23**), murine **CD23** was shown to bind to peritoneal macrophages and peripheral blood cells isolated from mice as well as the murine macrophage cell line, RAW. The interactions between mouse ZZ-**CD23** and CD11b/CD18-expressing cells were significantly inhibited by anti-CD11b monoclonal **antibodies**. A functional consequence was then demonstrated by inducing an up-regulation of interleukin-6 (IL-6) production following ZZ-**CD23** incubation with monocytes. The addition of Fab fragments generated from the monoclonal **antibody** CD11b impaired this cytokine production by 50%. Interestingly, a positive autocrine loop was identified as IL-6 was shown to increase **CD23** binding to macrophages. These results demonstrate that similar to findings using human cells, murine **CD23** binds to the surface adhesion molecule, CD11b, and these interactions regulate biological activities of murine myeloid cells.

L77 ANSWER 20 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

97377470 EMBASE Document No.: 1997377470. A new role for interleukin-7 in the induction of LFA-1 and VLA-4 adhesion molecules in Phorbol 12myristate 13acetate activated CD4+**CD23**+ T-cell subset. Fratazzi C.; Carini C.. Dr. C. Carini, Department of Tropical Public Health, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115, United States. Clinical and Experimental Allergy 27/11 (1335-1343) 1997. Refs: 49.
ISSN: 0954-7894. CODEN: CLEAEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Background: The low affinity receptor for IgE, **CD23**, has been described in several pathological conditions. However, the factors involved in the upregulation or downregulation of this receptor are still debated. Methods and Results: We studied the effect of interleukin 7 (IL-7) on the expression of **CD23** in normal PBT cells stimulated with PMA+Ca2. The data indicate that activated PB-T cultured in the presence of IL-7 showed an increased expression of **CD23**. The induction of IL-7 on **CD23** production appears to be independent of IL-2 IL-4, IL-9, IL-15. Indeed the addition of Specific MoAbs anti-IL-2, IL-4, IL-9, IL-15 or anti-IL2R was unable to block the effect of IL-7 on **CD23**. The addition of IL-7 to a specific subset cD4+ **CD23**+ was able to augment the adhesiveness of T cells to parenchymal cell monalayers. The use of different cytokine (IL-2, IL-4, IL-9, IL-15) resulted in no increase of adhesiveness. In contrast the + addition of IL-7 to a different T-cell subset (i.e. CD4 **CD23**-) was unable to rescue the lack of adhesiveness observed in these cells. **Blocking** experiments with MHM6 MoAb were able to drastically reduce the adhesiveness observed in CD4+**CD23**+ subsets. The presence of LFA-1 and VLA-4 adhesion molecules were responsible for the augmented adhesiveness of activated CD4+**CD23**+T Cells cultured in the presence of IL-7. **Blocking** experiments with anti-LFA-1, VLA-4, anti-LFA-1.beta. plus VLA-4.alpha. MoAbs or anti-ICAM-1 MoAb added to the monolayers resulted in a complete inhibition of adhesion to parenchyrnal monolayers. In contrast, the addition of anti-IL-7 or anti-IL-7R MoAbs were able to block the augmented adhesiveness of CD4+ **CD23**+ cells to monolayers observed in the presence of IL-7. Conclusion: Taken together these findings point to the likelihood that IL-7 is responsible for the observed quantitative difference in the level

of adhesion molecules and may open a new role of **CD23** in the immune regulation.

L77 ANSWER 21 OF 49 MEDLINE
97276838 Document Number: 97276838. PubMed ID: 9130531. Demonstration of the therapeutic potential of non-anaphylactogenic anti-IgE **antibodies** in murine models of skin reaction, lung function and inflammation. Heusser C H; Wagner K; Bews J P; Coyle A; Bertrand C; Einsle K; Kips J; Eum S Y; Lefort J; Vargaftig B B. (Asthma Allergy Research Department, Ciba Geigy Ltd., Basel, Switzerland.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1997 May-Jul) 113 (1-3) 231-5. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.
AB BACKGROUND: Allergies and allergic asthma are believed to be mediated by allergen-specific IgE **antibodies**. We have investigated the therapeutic potential of inhibiting endogenous IgE by a non-anaphylactogenic anti-mouse IgE **antibody** 1-5 with respect to its effects on antigen-induced skin reaction, lung function changes and lung inflammation in mice. METHODS: Mice were immunized with benzylpenicillinoyl-KLH or ovalbumin, and antigen-mediated skin reaction, bronchoconstriction, bronchopulmonary hyperresponsiveness (BHR) and lung eosinophilic inflammation determined in anti-IgE 1-5-treated versus untreated animals. RESULTS: Application of anti-IgE 1-5 inhibited (by 90%) the serum IgE and, 3-4 days after onset of treatment, blocked the antigen-induced skin reaction. Furthermore, the **antibody** also inhibited (by 90%) the antigen-induced infiltration of eosinophils into the lung. This latter effect seems to be mediated by **blocking** the IgE-**CD23** interaction and indicates that lung eosinophilic inflammation also depends on IgE. Moreover, when applied to rats passively sensitized with mouse IgE, **antibody** 1-5 inhibited the antigen-induced bronchoconstriction. A similar effect could be seen in actively immunized mice, where **antibody** 1-5 was able to inhibit (by 70%) the ovalbumin-induced bronchoconstriction as well as BHR. CONCLUSIONS: In summary, non-anaphylactogenic anti-IgE **antibodies** can markedly inhibit IgE levels and IgE-mediated allergic reactions. Since bronchoconstriction, BHR and lung eosinophilic inflammation can be suppressed, such **antibodies** may be attractive principles for the treatment of allergic asthma.

L77 ANSWER 22 OF 49 MEDLINE
96245984 Document Number: 96245984. PubMed ID: 8698393. CD40 **antibodies** defining distinct epitopes display qualitative differences in their induction of B-cell differentiation. Bjorck P; Paulie S. (Department of Immunology, Stockholm University, Sweden.) IMMUNOLOGY, (1996 Feb) 87 (2) 291-5. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.
AB IgE production can be obtained in vitro by stimulating B lymphocytes with CD40 **antibodies** and interleukin-4 (IL-4). This stimulation also results in homotypic aggregation and cell proliferation. We have shown previously that IgE synthesis may be dependent on additional signals provided by the close cellular contact. Thus inhibition of the aggregation by lymphocyte function-associated antigen-1 (LFA-1) **antibodies** leads to a decrease in IgE production. In the present study we show that the inhibitory effect of LFA-1 **antibodies** is critically dependent on the CD40 **antibody** used for stimulation. Thus, while previously using the monoclonal **antibody** (mAb) S2C6, IgE production induced by the CD40 **antibody** mAb89 was generally higher and could be enhanced more than fivefold in the presence of LFA-1 **antibodies**. Similarly, the addition of the **CD23** mAb MHM6, which blocked aggregation to a similar degree as the LFA-1 **antibodies**, inhibited S2C6-induced IgE production but enhanced that induced by mAb89. In contrast to these opposing effects on IgE synthesis, proliferation induced by the two CD40 **antibodies** was affected similarly by the **blocking antibodies**. As the

interaction between **CD23** and CD21 has been suggested to involve recognition of carbohydrate structures on CD21 by the lectin-like domain on **CD23**, we also tested the effect of some different sugars on IgE synthesis and proliferation. Addition of fucose-1-phosphate to anti-CD40 and IL-4-stimulated B cells completely inhibited IgE synthesis and proliferation. Inhibition was also seen with mannose-6-phosphate but not with glucose-1-phosphate. In contrast to the MHM6 **antibody**, the effect of the sugars was similar irrespective of the CD40 **antibody** used for stimulation. The study shows that different **antibodies** to CD40 may give rise to qualitatively distinct signals depending on the epitope recognized.

L77 ANSWER 23 OF 49 SCISEARCH COPYRIGHT 2003 ISI (R)
96:893563 The Genuine Article (R) Number: VV268. Interleukin-7 modulates intracytoplasmatic **CD23** production and induces adhesion molecule expression and adhesiveness in activated CD4(+)**CD23**(+) T cell subsets. Fratazzi C (Reprint); Carini C. HARVARD UNIV, SCH MED, DEPT MED, BOSTON, MA 02115 (Reprint); HARVARD UNIV, SCH PUBL HLTH, DEPT CANC BIOL, BOSTON, MA 02115. CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY (DEC 1996) Vol. 81, No. 3, pp. 261-270. Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS. 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495. ISSN: 0090-1229. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The low-affinity receptor for IgE, **CD23**, has been described in several pathological conditions. However, the factors involved in the upregulation or downregulation of this receptor are still debated. We studied the effect of interleukin 7 (IL-7) on the production of **CD23** in normal PET cells stimulated with PIMA + Ca-2. The results demonstrate that cytoplasmic **CD23** level was significantly augmented by costimulation with PMA + Ca-2 plus IL-7 (1000 U/ml). Using an intracytoplamatic cytometric analysis, an accumulation of intracellular **CD23** was observed at 48 hr in the presence of IL-7. This appears to have a profile different from the **CD23** surface expression peaking at 72 hr of culture. We were also able to show that sCD23 was specifically increased by IL-7 and occurred with an early peak at 72 hr and a late peak at 120 hr of culture. The increased release and the biphasic production of sCD23 may reside in an accelerated degradation of the receptor due to an excessive accumulation of it. Restimulation of CD4(+) T cells with PMA + Ca-2 without IL-7 changed the profile of sCD23 production showing a second peak at 144 hr of culture. The induction of IL-7 on **CD23** production appears to be independent of IL-2, IL-4, IL-9, and IL-15. Indeed, the addition of specific mAbs anti-IL-2, -IL-4, -IL-9, -IL-15, or anti-IL-2R was unable to block the effect of IL-7 on **CD23**. The addition of IL-7 to specific subset CD4(+)**CD23**(+) was able to augment the adhesiveness of T cells to parenchymal cell monolayers. The use of different cytokine (IL-2, IL-4, IL-9, IL-15) resulted in no increase of adhesiveness. In contrast, the addition of IL-7 to a different T cell subset (i.e., CD4(+)**CD23**(-)) was unable to rescue the lack of adhesiveness observed in these cells. The adhesion molecules LFA-1 and VLA-4 were responsible for the augmented adhesiveness of activated CD4(+)**CD23**(+) T cells cultured in the presence of IL-7. **Blocking** experiments with anti-LFA-1 beta, VLA-4 alpha, anti-LFA-lp plus VLA-4 alpha mAbs, or anti-ICAM-1 mAb added to the monolayers resulted in a complete inhibition of adhesion to parenchymal monolayers. In contrast, the addition of anti-IL-7 or anti-IL-7R. mAbs was able to block the augmented adhesiveness of CD4(+)**CD23**(+) cells to monolayers observed in the presence of IL-7. A significant augmentation of LFA-1 and VLA-4 was observed in cells cultured in the presence of IL-7. Taken together these findings point to the likelihood that IL-7 is responsible for the observed quantitative difference in the level of adhesion molecules and may open a new role of **CD23** in the immune regulation. (C) 1996 Academic Press, Inc.

L77 ANSWER 24 OF 49 MEDLINE

96152742 Document Number: 96152742. PubMed ID: 8566063. Nerve growth-factor and anti-CD40 provide opposite signals for the production of IgE in interleukin-4-treated lymphocytes. Brodie C; Oshiba A; Renz H; Bradley K; Gelfand E W. (Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206, USA.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jan) 26 (1) 171-8. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Nerve growth factor (NGF) is a well-known neurotrophic factor acting on both the peripheral and the central nervous systems. In addition, it has been shown to play a role in the function of the immune system through specific receptors. Both high-affinity and low-affinity NGF receptors (NGFR) are expressed on human B lymphocytes. The low-affinity NGFR has been shown to have structural homology with another specific B cell surface molecule, CD40, which plays an important role in IgE production. In view of the structural similarities of the p75 NGFR and CD40 we examined whether NGF may also be involved in the regulation of IgE production. We found that NGF and anti-CD40 exerted opposite effects on the induction of IgE by IL-4 in peripheral blood mononuclear cells. NGF inhibited the induction of IgE by IL-4 and this inhibition was not mediated through **blocking** of the induction of **CD23** nor through inhibition of IL-4R expression. The inhibition of IL-4-dependent IgE production was observed on surface (s)IgE+ and sIgE-/sIgM+ B lymphocytes. Anti-CD40 on the other hand, exerted an enhancing effect on IgE production and its addition to IL-4 provided a signal that was resistant to the inhibitory effect of NGF. Antagonistic effects of NGF and IL-4 were also observed for other Ig isotypes since IL-4 prevented the increase in IgA and IgM production induced by NGF. These data indicate that although NGFR and CD40 belong to the same receptor superfamily and exert similar proliferative effects on B lymphocytes, they interact differently with IL-4 in the regulation of IgE production.

L77 ANSWER 25 OF 49 MEDLINE

97051448 Document Number: 97051448. PubMed ID: 8896174. A novel monoclonal **antibody** mNI-58A against the alpha-chain of leukocyte function-associated antigen-1 (LFA-1) blocks the homotypic cell aggregation and actively regulates morphological changes in the phorbol myristate acetate (PMA)-activated human monocyte-like cell line, U937. Ikewaki N; Yamada A; Sonoda A; Inoko H. (Department of Microbiology, Kitasato University School of Nursing, Kanagawa, Japan.) TISSUE ANTIGENS, (1996 Sep) 48 (3) 161-73. Journal code: 0331072. ISSN: 0001-2815. Pub. country: Denmark. Language: English.

AB A monoclonal **antibody** (mAb), designated mNI-58A, was produced by immunizing mice with the lipopolysaccharide (LPS)-stimulated monocyte-like cell line, U937. The antigen defined by mNI-58A was widely expressed on various lymphoid cells and all cell lines examined except the erythroid cell line, K562. When the reactive patterns between mNI-58A and the mAbs to various human differentiation antigens (CD11a, CD11b, CD11c, CD14, CD16, CD18, **CD23**, CD28, CD29, CD31, CD43, CD44, CD45RA, CD50, CD54, CD58, CD80, CD102, CD106, HLA-class I and-class II antigen) were compared, that of mNI-58A was found to be similar to those of the leukocyte function-associated antigen-1 (LFA-1) mAbs. Using a competitive immunofluorescence binding assay it was found that the preincubation with one of the CD11a mAbs, 2F12 completely blocked the subsequent binding of mNI-58A. mNI-58A prevented the homotypic cell aggregation of the phorbol myristate acetate (PMA)-activated U937 cells (referred to as PMA-U937) and PMA-activated Epstein-Barr virus (EBV)-transformed B cell lines, B-85 and Mann. mNI-58A markedly induced the spread formation of the PMA-U937 cells following this **blocking** of the homotypic cell aggregation, whereas 2F12 did not under the same condition. The spread formation induced by mNI-58A was completely blocked by cytochalasin B (CyB), cytochalasin D (CyD), cycloheximide (CHX) or protein kinase C inhibitors,

sphingosine and H-7. The U937 cells markedly adhered to the tumor necrosis factor-alpha (TNF-alpha)-stimulated human umbilical vein endothelial cells (HUVECs) and also to the extracellular matrix protein, fibronectin, but mNI-58A did not enhance or block these adhesion process. mNI-58A precipitated two glycoproteins with molecular weight 180 kDa and 95 kDa as determined by SDS-PAGE analysis, which were identical to the LFA-alpha (CD11a) and beta (CD18) chains of leukocyte integrin precipitated by the CD11a mAbs, respectively. Sequential immunoprecipitation studies using the CD11a mAb (2F12) also indicate that mNI-58A recognizes an epitope on the alpha-chain of the LFA-1 molecule. The ability of mNI-58A to block the PMA-U937 cells and to induce the spread formation of these cells suggests that mNI-58A is a novel mAb reacting with an epitope on the alpha-chain of LFA-1 different from those recognized with the existing CD11a mAbs.

L77 ANSWER 26 OF 49 MEDLINE

97056193 Document Number: 97056193. PubMed ID: 8900533. Role of IgE immune complexes in the regulation of HIV-1 replication and increased cell death of infected U1 monocytes: involvement of **CD23**/Fc epsilon RII-mediated nitric oxide and cyclic AMP pathways. Ouaaz F; Ruscetti F W; Dugas B; Mikovits J; Agut H; Debre P; Mossalayi M D. (Molecular Immuno-hematology Group, CNRS URA625, Pitie-Salpetriere Hospital, Paris, France.) MOLECULAR MEDICINE, (1996 Jan) 2 (1) 38-49. Journal code: 9501023. ISSN: 1076-1551. Pub. country: United States. Language: English.

AB BACKGROUND: IgE/anti-IgE immune complexes (IgE-IC) induce the release of multiple mediators from monocytes/macrophages and the monocytic cell line U937 following the ligation of the low-affinity Fc epsilon receptors (Fc epsilon RII/**CD23**). These effects are mediated through an accumulation of cAMP and the generation of L-arginine-dependent nitric oxide (NO). Since high IgE levels predict more rapid progression to acquired immunodeficiency syndrome, we attempted to define the effects of IgE-IC on human immunodeficiency virus (HIV) production in monocytes. MATERIALS AND METHODS: Two variants of HIV-1 chronically infected monocytic U1 cells were stimulated with IgE-IC and virus replication was quantified. NO and cAMP involvement was tested through the use of agonistic and antagonistic chemicals of these two pathways. RESULTS: IgE-IC induced p24 production by U1 cells with low-level constitutive expression of HIV-1 mRNAs and extracellular HIV capsid protein p24 levels (U1low), upon their pretreatment with interleukin 4 (IL-4) or IL-13. This effect was due to the crosslinking of **CD23**, as it was reversed by **blocking** the IgE binding site on **CD23**. The IgE-IC effect could also be mimicked by crosslinking of **CD23** by a specific monoclonal **antibody**. p24 induction by IgE-IC was then shown to be due to **CD23**-mediated stimulation of cAMP, NO, and tumor necrosis factor alpha (TNF alpha) generation. In another variant of U1 cells with > 1 log higher constitutive production of p24 levels (U1high), IgE-IC addition dramatically decreased all cell functions tested and accelerated cell death. This phenomenon was reversed by **blocking** the nitric oxide generation. CONCLUSIONS: These data point out a regulatory role of IgE-IC on HIV-1 production in monocytic cells, through **CD23**-mediated stimulation of cAMP and NO pathways. IgE-IC can also stimulate increased cell death in high HIV producing cells through the NO pathway.

L77 ANSWER 27 OF 49 SCISEARCH COPYRIGHT 2003 ISI (R)

96:369839 The Genuine Article (R) Number: UJ686. THE EPSTEIN-BARR VIRUS-BINDING SITE ON CD21 IS INVOLVED IN **CD23** BINDING AND INTERLEUKIN-4-INDUCED IGE AND IGG4 PRODUCTION BY HUMAN B-CELLS. HENCHOZLECOANET S; JEANNIN P; AUBRY J P; GRABER P; BRADSHAW C G; POCHON S; BONNEFOY J Y (Reprint). GLAXO INST MOLEC BIOL, DEPT IMMUNOL, 14 CHEMIN AULX, CASE POSTALE 674, 1228 PLAN OUATES, GENEVA, SWITZERLAND (Reprint); GLAXO INST MOLEC BIOL, DEPT IMMUNOL, GENEVA, SWITZERLAND. IMMUNOLOGY (MAY 1996) Vol. 88, No. 1, pp. 35-39. ISSN: 0019-2805. Pub. country:

SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human CD21 has previously been described as a receptor for the C3d,g and iC3b proteins of complement, as a receptor for the gp350/220 envelope glycoprotein of the Epstein-Barr virus (EBV) and also as a receptor for interferon-alpha (IFN-alpha). Structurally, CD21 consists of 15 to 16 short consensus repeats (SCR) of 60 to 75 amino acids followed by a transmembrane domain and an intracytoplasmic region. We reported that **CD23**, a low-affinity receptor for IgE (Fc epsilon R2), is a new functional ligand for CD21. We recently found that the sites of interaction of **CD23** on CD21 are on SCR 5 to 8 and 1-2. The first site is a lectin-sugar type of interaction and the second site is a protein-protein interaction. We report here that amongst the other ligands for CD21 (EBV, C3d,g and IFN-alpha), only EBV is able to inhibit the binding of **CD23** to CD21. Furthermore, even a peptide from gp350/220 of EBV known to bind to CD21 is able to decrease **CD23** binding to CD21. Since **CD23**/CD21 pairing is important in the control of IgE production, we tested the effect of the EBV-derived peptide on immunoglobulin production from peripheral blood mononuclear cells and purified tonsillar B cells. Interestingly, the EBV-peptide inhibited IgE and IgG4 production induced by interleukin-4, in a dose-dependent manner. The same results were obtained using either peripheral blood mononuclear cells or purified tonsillar B cells. Another CD21 ligand, C3, did not affect binding of **CD23** to CD21 nor the production of IgE and IgG4. This study indicates that **blocking CD23** binding to CD21 SCR 2 on human B cells selectively modulates immunoglobulin production.

L77 ANSWER 28 OF 49 MEDLINE

95299158 Document Number: 95299158. PubMed ID: 7780154. Expression of CD21 antigen on myeloma cells and its involvement in their adhesion to bone marrow stromal cells. Huang N; Kawano M M; Mahmoud M S; Mihara K; Tsujimoto T; Niwa O; Kuramoto A. (Department of Hematology and Oncology, Hiroshima University, Japan.) BLOOD, (1995 Jun 15) 85 (12) 3704-12. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB The mature myeloma cells express very late antigen 5 (VLA-5) and MPC-1 antigens on their surface and adhere to bone marrow (BM) stromal cells more tightly than the VLA-5-MPC-1- immature myeloma cells in vitro. The VLA-5 and MPC-1 antigens possibly function as two of the molecules responsible for interaction of mature myeloma cells with BM stromal cells. However, the immature myeloma cells do interact with BM stromal cells, and it is unclear which adhesion molecules mediate their interaction. In this study, we found that both immature and mature myeloma cells expressed CD21, an adhesion molecule known to bind to **CD23**. CD21 was also detected on normal plasma cells. To evaluate the role of CD21 expression on myeloma cells, two myeloma cell lines, NOP-2 (VLA-5-MPC-1-) and KMS-5 (VLA-5+MPC-1+), were used as representatives of immature and mature myeloma cell types, respectively, and an adhesion assay was performed between the myeloma cell lines and BM stromal cells. **Antibody-blocking** results showed that adhesion of the mature type KMS-5 to KM102, a human BM-derived stromal cell line, or to short-term cultured BM primary stromal cells was inhibited by monoclonal **antibodies** (MoAbs) against CD21, VLA-5, and MPC-1, and inhibition of adhesion of the immature type NOP-2 to KM102 by the anti-CD21 MoAb was observed as well. Furthermore, **CD23** was detected on KM102. Treatment of KM102 with an anti-**CD23** MoAb also inhibited adhesion of either KMS-5 or NOP-2 to KM102. Therefore, we propose that CD21 expressed on myeloma cells likely functions as a molecule responsible for the interaction of immature myeloma cells as well as mature myeloma cells with BM stromal cells, and **CD23** may be the ligand on the stromal cells for the CD21-mediated adhesion.

L77 ANSWER 29 OF 49 MEDLINE
95293053 Document Number: 95293053. PubMed ID: 7774652. No role of interleukin-4 in **CD23**/IgE-mediated enhancement of the murine **antibody** response in vivo. Hjulstrom S; Landin A; Jansson L; Holmdahl R; Heyman B. (Department of Pathology, Uppsala University Hospital, Sweden.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 May) 25 (5) 1469-72. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Antigen-specific IgE up-regulates the specific IgM, IgG1, IgG2a and IgE response in vivo when given to mice together with antigen. The enhancement is mediated by the low-affinity receptor for IgE, Fc epsilon RII or **CD23**, as demonstrated both in **CD23**-deficient mice and by **blocking** **CD23** with anti-**CD23** monoclonal **antibodies**. A possible mechanism behind the regulatory effects of **CD23** is that the IgE/**CD23** /antigen complex is endocytosed by B cells, leading to increased antigen processing and presentation on major histocompatibility complex (MHC) class II molecules to T helper cells. In the present study we have found that the expression of **CD23** is reduced fivefold on splenic B cells in mice genetically deficient for IL-4. When IL-4-deficient mice and normal littermates were immunized with 2,4,6-trinitrophenyl (TNP)-specific IgE followed by bovine serum albumin (BSA)-TNP or with BSA-TNP alone, the BSA-specific IgG1 and IgG2a responses were equally well augmented by IgE in all mice. In addition, a low but significant IgE response was seen even in the IL-4-deficient mice. Thus, enhancement of the **antibody** response through IgE and **CD23** occur in the absence of IL-4 and is not dependent on **CD23** up-regulation.

L77 ANSWER 30 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
95073119 EMBASE Document No.: 1995073119. Cytokine monitoring of infection and rejection in renal transplant recipients. Daniel V.; Pasker S.; Wiesel M.; Carl S.; Pomer S.; Staehler G.; Schnobel R.; Weimer R.; Opelz G.. Dept. of Transplantation Immunology, Institute of Immunology, Im Neuenheimer Feld 305,D-69120 Heidelberg, Germany. Transplantation Proceedings 27/1 (884-886) 1995.
ISSN: 0041-1345. CODEN: TRPPA8. Pub. Country: United States. Language: English.

L77 ANSWER 31 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
94110943 EMBASE Document No.: 1994110943. Granulocyte-macrophage colony-stimulating factor stimulates macrophages to respond to IgE via the low affinity IgE receptor (**CD23**). Matz J.; Williams J.; Rosenwasser L.J.; Borish L.C.. Natl. Jewish Center for Immunology, 1400 Jackson St.,Denver, CO 80206, United States. Journal of Allergy and Clinical Immunology 93/3 (650-657) 1994.
ISSN: 0091-6749. CODEN: JACIBY. Pub. Country: United States. Language: English. Summary Language: English.

AB We have found increased concentrations of granulocyte-macrophage colony-stimulating factor (GM-CSF) in the bronchoalveolar lavage fluid of 11 patients with nocturnal asthma (15.3 .+-. 4.6 pg/ml) compared with normal subjects (2.3 .+-. 6.1 pg/ml) ($p = 0.03$). In contrast to patients with asthma, low affinity IgE receptors (Fc.epsilon.RII or **CD23**) are not expressed on monocytes obtained from healthy, nonatopic donors. Fc.epsilon.RII expression was induced by the cytokines GM-CSF and interleukin (IL)-4 either alone or in combination. As assessed by flow cytometry, the combination of IL-4 and GM-CSF was found to be synergistic, inducing up to 54.8% .+-. 4.6% Fc.epsilon.RII-positive monocytes compared with a maximum of 27.4% .+-. 5.0% and 30.0% .+-. 4.0% with IL-4 and GM-CSF alone, respectively ($p < 0.05$ compared with either cytokine alone). Human monocytes from the peripheral blood of seven normal subjects were cultured for 24 hours with and without IL-4 or GM-CSF. With IL-4, addition of IgE/anti-IgE complexes failed to induce IL-1 secretion and inhibited IL-1 secretion induced by lipopolysaccharides. The addition of GM-CSF or

IgE immune complexes alone resulted in no additional IL-1 secretion in supernatants of the untreated monocytes, whereas the IgE complexes did stimulate IL-1 secretion by monocytes cultured in GM-CSF, as measured by ELISA (from 0.7 .+-. 0.2 ng/ml to 2.3 .+-. 0.5 ng/ml; p < 0.01). This could be confirmed to represent an Fc.epsilon.RII-dependent process insofar as **blocking** of the Fc.epsilon.RII receptors abrogated the capacity of the IgE complexes to induce IL-1.beta. (1.0 .+-. 0.4 ng/ml IL-1; p = NS in comparison with untreated monocytes). We conclude that GM-CSF is increased in the bronchoalveolar lavage fluid of patients with asthma and may be important in macrophage activation via induction of the low affinity IgE receptor, thereby making cells susceptible to IgE-dependent activation.

L77 ANSWER 32 OF 49 MEDLINE

94065186 Document Number: 94065186. PubMed ID: 8245470. Antigen-dependent stimulation by bone marrow-derived mast cells of MHC class II-restricted T cell hybridoma. Frandji P; Oskeritzian C; Cacaraci F; Lapeyre J; Peronet R; David B; Guillet J G; Mecheri S. (Unite d'Immuno-Allergie, Institut Pasteur, Paris, France.) JOURNAL OF IMMUNOLOGY, (1993 Dec 1) 151 (11) 6318-28. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB This paper describes a new role for mast cells as being able to present Ag to immune T cells. A mouse bone marrow-derived mast cell population obtained after 3 wk of culture in a conditioned medium has been shown to express a variety of membrane-associated Ag, including MHC class II and class I Ag, **CD23**, CD32, high affinity receptor for IgE, and CD4. Expression of MHC class II molecules was up-regulated upon stimulation with LPS but not with IFN-gamma and was down-regulated after exposure of mast cells to IL-3 treatment. We have demonstrated that mast cells were able to present native Ag as well as immunogenic peptides to MHC class II-restricted T cell hybridoma. The inhibition of Ag presentation after mast cells have been treated with ammonia suggests that Ag catabolism in intracytoplasmic compartment as a key step in Ag handling takes place in these cells. The MHC class II molecule is the restricting element for the presentation of OVA and the lambda repressor from bacteriophage lambda to a panel of specific T cell hybridomas, as demonstrated by the **blocking** effect of anti-MHC class II mAb on the Ag-presenting function. A characteristic feature of mast cells is the generation of a narrower immunogenic peptide repertoire as compared with A20 and LBB 3.4.16, a B lymphoma cell line, and a B cell hybridoma, respectively. This novel function of mast cells brings to a much closer connection inflammatory and immunologic processes and sheds new light on the biology of mast cells and particularly on the specific allergic responses.

L77 ANSWER 33 OF 49 MEDLINE

93271485 Document Number: 93271485. PubMed ID: 8499634. Identification of a distinct low-affinity receptor for human interleukin-4 on pre-B cells. Fanslow W C; Spriggs M K; Rauch C T; Clifford K N; Macduff B M; Ziegler S F; Schooley K A; Mohler K M; March C J; Armitage R J. (Immunex Research and Development Corp., Seattle, WA 98101.) BLOOD, (1993 Jun 1) 81 (11) 2998-3005. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB Biotinylated interleukin-4 (IL-4) was used to examine IL-4 receptor (IL-4R) expression on a range of human B-cell lines by flow cytometry. Using high concentrations of biotinylated IL-4, we have identified a novel low-affinity IL-4 receptor expressed at high levels on pre-B lines. Expression of this low-affinity receptor did not correlate with detected mRNA levels for the previously cloned receptor or with reactivity of two anti-human IL-4R monoclonal **antibodies** (MoAb). Radiolabeled IL-4 cross-linking studies using pre-B lines showed a doublet of 65 to 75 Kd in contrast to the 110- to 130-Kd molecule detected on cells expressing the cloned IL-4R. A soluble IL-4 binding protein (IL-4bp) was purified from the supernatants of three pre-B lines expressing the low-affinity

receptor on their surface. IL-4bp could block both IL-4-mediated **CD23** induction on tonsil B cells and IL-4-induced inhibition of proliferation of the pre-B line JM1. Partial N-terminal amino acid sequence was obtained from purified IL-4bp that confirmed this protein to be novel. A 12 amino acid peptide based on the IL-4bp sequence was used to produce a polyclonal antiserum that was reactive with purified IL-4bp, and also bound to the surface of pre-B cells but not to murine CTLL cells transfected with the human IL-4R. **Blocking** MoAb against the previously characterized high-affinity receptor inhibited IL-4-mediated proliferation of hIL-4R+ CTLL cells but had no effect on IL-4-induced inhibition of JM1 cell proliferation, and only partially inhibited IL-4-mediated **CD23** and sIgM induction and proliferation of tonsil B cells. The data presented here provide evidence for a novel cell-surface expressed low-affinity IL-4R that also exists as a biologically active soluble IL-4 binding protein.

L77 ANSWER 34 OF 49 MEDLINE

93286342 Document Number: 93286342. PubMed ID: 8509581. Pokeweed mitogen induces IgE synthesis in the presence of a **blocking antibody** to the interferon-gamma receptor. Jujo K; Renz H; Abe J; Trumble A; Gelfand E W; Leung D Y. (Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1993 Jun) 91 (6) 1206-16. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Although pokeweed mitogen (PWEM) can induce peripheral blood mononuclear cells (PBMCs) to synthesize IgG, IgA, and IgM, such cultures fail to induce IgE synthesis. The present study examined the possibility that the stimulation of interferon-gamma (IFN-gamma) production plays a role in the failure of PWM to induce IgE synthesis. METHODS: We examined PBMCs from eight normal control subjects for IFN-gamma and IL-4 production. Since IFN-gamma synthesis is known to inhibit IgE synthesis, we also examined the effect of a neutralizing anti-IFN-gamma **antibody** and of two anti-IFN-gamma receptor **antibodies,** monoclonal **antibody** (mAb) GIR208, which blocks cellular binding of IFN-gamma, and mAB GIR94.5, which binds to the IFN-gamma receptor but does not block the binding of IFN-gamma to its receptor on PWM-stimulated PBMCs. RESULTS: After stimulation with PWM, culture supernatants contained significantly more IFN-gamma ($p = 0.001$) and IL-4 ($P = 0.001$) compared with supernatants from nonstimulated cultures. PWM-stimulated PBMCs also expressed higher levels of IFN-gamma and IL-4 gene transcripts than unstimulated cells. When cultured in the presence of anti-IFN-gamma, supernatants from PWM-stimulated cultures also induced **CD23** on Ramos B cells in an IL-4-dependent manner. In the presence of mAB GIR208 and a neutralizing anti-IFN-gamma **antibody,** but not mAb GIR94.5, PWM stimulated PBMCs from eight normal control subjects and six patients with atopic dermatitis to produce IgE. Monoclonal **antibody** GIR208, however, did not enhance IgG synthesis. Furthermore, the exogenous addition of IFN-gamma inhibited the IgE-stimulatory effect of mAb GIR208. Monoclonal **antibody** GIR208 was unable to induce purified B cells to synthesize IgE in the presence of IL-4. CONCLUSIONS: Thus unlike anti-CD40, mAb GIR208 does not act as a second signal for the induction of IgE synthesis. These results demonstrate that the induction of IFN-gamma production contributes to the failure of PWM to stimulate synthesis of IgE in PBMCs from atopic and nonatopic donors.

L77 ANSWER 35 OF 49 SCISEARCH COPYRIGHT 2003 ISI (R)

93:475155 The Genuine Article (R) Number: LP127. INTERLEUKIN-4 PRIMING ENHANCES A TARGET FOR HUMAN COMPLEMENT-MEDIATED CYTOTOXICITY OF CLL. CZUCZMAN M S; CLASS K; SCHEINBERG D A (Reprint). MEM SLOAN KETTERING CANC CTR, HEMATOPOIET CANC IMMUNOCHEM LAB, 1275 YORK AVE, NEW YORK, NY, 10021. LEUKEMIA (JUL 1993) Vol. 7, No. 7, pp. 1020-1025. ISSN: 0887-6924. Pub. country: USA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB JD118 is a murine immunoglobulin M monoclonal **antibody** (mAb) under study as a therapeutic agent thal is capable of potent human complement-mediated cytotoxicity (CMC) against B-cell lymphoma and leukemia targets. The JD118 antigen target was upregulated on fresh human B cells and B-cell neoplasms after brief in vitro incubation in media containing calf serum. To determine if cytokines could also lead to upregulation of JD118 antigen, alpha-interferon (alpha-IFN), gamma-interferon (gamma-IFN), interleukin 2 (IL-2), or IL-4 were added to fresh neoplastic 8 cells in serum-free media and changes in JD118 antigen expression were evaluated by flow cytometry (FCM). IL-4 was found to be the predominant cytokine responsible for inducing upregulation of the JD118 antigen. Marked JD118 upregulation by IL-4 was seen in 14 out of 14 chronic lymphocytic leukemia (CLL) samples tested, with 50 to 750-fold increases in four samples, 11 to 49-fold increases in four samples, and up to 10-fold increase in six samples. One B-cell lymphoma specimen was upregulated 18-fold, but no upregulation was demonstrated in one hairy cell leukemia and two acute myelogenous leukemia specimens tested. The specificity of the IL-4 upregulation was demonstrated by the elimination of its activity by **blocking** with a neutralizing anti-IL-4 mAb. IL-4 upregulation allows JD11 8 mAb CMC against otherwise antigen-negative targets and argues for phase I trials using a combination of IL-4 cytokine and mAb for B-cell neoplasms.

L77 ANSWER 36 OF 49 MEDLINE

93318718 Document Number: 93318718. PubMed ID: 7687088. A study of the interrelationship between circulating IgG subclass anti-IgE autoantibodies, IgE and soluble **CD23** in asthma. Shakib F; Boulstridge L; Smith S J. (Department of Immunology, University Hospital, Queen's Medical Centre, Nottingham, U.K.) ALLERGOLOGIA ET IMMUNOPATHOLOGIA, (1993 Jan-Feb) 21 (1) 20-4. Journal code: 0370073. ISSN: 0301-0546. Pub. country: Spain. Language: English.

AB In this paper we hypothesise that circulating autoanti-IgE **antibodies**, which are found in allergic asthma patients, could potentially enhance IgE synthesis by **blocking** its binding to **CD23** on B lymphocytes, thereby potentiating the release of soluble fragments of **CD23** which have B cell growth-promoting activity. We have investigated this possibility indirectly by measuring soluble (s) **CD23** and IgG subclass anti-IgE **antibody** levels in asthmatic patients' sera, to find out if the two parameters are related. However, we were unable to show any significant correlations between serum IgG subclass anti-IgE activities and sCD23 levels. This may have been due, at least in part, to the heterogeneous epitope specificity of the autoanti-IgE being detected. Interestingly, there was a significant inverse correlation ($p = 0.0178$) between serum IgE and sCD23 levels in asthma; an observation which underlines the notion that binding of IgE to membrane **CD23** abrogates the release of sCD23. The present study confirms and extends previous reports of significantly raised circulating levels of IgG anti-IgE in asthma patients ($p = 0.0004$), by further demonstrating that IgG anti-IgE is mostly restricted to IgG1. Given that IgG1 binds very efficiently to C1q and Fc gamma Rs, our observation lends further support to the notion that IgG anti-IgE may facilitate the removal of IgE-allergen complexes by triggering IgG effector function pathways.

L77 ANSWER 37 OF 49 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

93121689 EMBASE Document No.: 1993121689. [sCD23 and sIL-2R in allergic children receiving immunotherapy during 18 months]. SCD23 Y SIL-2R EN NINOS ALERGICOS RECIBIENDO INMUNOTERAPIA DURANTE DIECIOCHO MESES. Blanco Quiros A.; Garrote Adrados J.A.; Lapena Lopez De Armendia S.; Andion Dapena R.; Linares Lopez P.. Facultad de Medicina, Pediatria, Ramon y Cajal 5,47005 Valladolid, Spain. Revista Espanola de Alergologia e Inmunologia Clinica 8/1 (17-24) 1993.
ISSN: 0214-1477. CODEN: REACEN. Pub. Country: Spain. Language: Spanish.

Summary Language: Spanish; English.

AB The variations on total IgE, serum soluble interleukin-2 receptor (sIL-2R) and low affinity IgE (sCD23) due to immunotherapy (IT) were studied. Twenty-four children allergic to pollen or dermatophagoides were included; 16 patients were treated with IT and 8 only received symptomatic therapy or environmental control measures. Blood samples were collected before starting the treatment and they were repeated in all cases 18 months afterwards. In patients not treated with IT there was an increase of IgE ($p < 0.05$) and a decrease of sCD23 (p:0.023), whereas in children who received IT there were no significant changes. A mild decrease of sIL-2R was produced in both groups, but it was not significant. Before starting IT, there was a correlation between IgE and sIL-2R (p:0.19) and a lesser one between IgE and sCD23 (p: 0.065) but it disappeared after 18 months' IT. The sCD23 levels decrease very much during childhood and the IT seems to diminish this trend. Larger and longer studies will be needed to assess whether IT increases the sCD23 levels and whether these molecules have any anti-allergic function **blocking** the circulant IgE **antibodies**; nevertheless children are not the more convenient patients for these assays, due to normal IgE increase and sCD23 decrease produced along the childhood. There was not any difference in the 3 studied factors, neither before nor after the IT. In spite of previous hypotheses, sCD23 and sIL-2R do not seem very useful for monitoring the outcome of IT.

L77 ANSWER 38 OF 49 MEDLINE

93049182 Document Number: 93049182. PubMed ID: 1385115. Cytokine effects of **CD23** are mediated by an epitope distinct from the IgE binding site. Mossalayi M D; Arock M; Delespesse G; Hofstetter H; Bettler B; Dalloul A H; Kilchherr E; Quaaz F; Debre P; Sarfati M. (Groupe d'Immuno-Hematologie Moleculaire, CHU Pitie-Salpetriere, Paris, France.) EMBO JOURNAL, (1992 Dec) 11 (12) 4323-8. Journal code: 8208664. ISSN: 0261-4189. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Human **CD23** and its soluble forms (sCD23) display various biological activities, in addition to their IgE binding function (IgE/BF). The IgE binding domain was recently mapped to residues between Cys163 and Cys282 but its involvement in IgE-independent, **CD23** functions remains unknown. In order to clarify this point, a series of N-terminal, C-terminal and internal deletion mutants of **CD23** or sCD23 were expressed in CHO cells and tested for their ability (i) to bind to IgE, (ii) to induce colony formation by human myeloid precursor cells, (iii) to promote mature T cell marker expression by early prothymocytes, and (iv) to regulate IgE synthesis. The present study indicates that cytokine activities require the presence of Cys288, while this amino acid is not necessary for IgE/BF. **Blocking** experiments using various conformation-sensitive monoclonal **antibodies** further suggest that active epitope(s) of **CD23** in cytokine assays is(are) distinct from those involved in IgE/BF.

L77 ANSWER 39 OF 49 MEDLINE

93016851 Document Number: 93016851. PubMed ID: 1401061. Epidermal keratinocyte-derived basophil promoting activity. Role of interleukin 3 and soluble **CD23**. Dalloul A H; Arock M; Fourcade C; Beranger J Y; Jaffray P; Debre P; Mossalayi M D. (Laboratoire d'Immunologie, Centre National de la Recherche Scientifique URA625, CHU Pitie-Salpetriere, Paris, France.) JOURNAL OF CLINICAL INVESTIGATION, (1992 Oct) 90 (4) 1242-7. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Human epidermal keratinocytes (EK) secrete factors able to sustain the proliferation of early myeloid cells and, in particular, the generation of basophils. This activity was previously attributed to IL-3, although no definitive in situ demonstration of this cytokine was provided. In regard to the possible physiological relevance of these data, we investigated herein the nature of EK-derived factors responsible for basophil

promotion. Our data show that EK-derived supernatants (EK-sup) contain IL-3 as well as soluble **CD23** (sCD23), both known for their colony stimulating activity. Messenger RNA for IL-3 and **CD23** were also detected in EK. **Blocking** experiments using specific neutralizing monoclonal **antibodies** (mAb) further indicate that EK-derived basophil promoting activity is mainly due to the presence of IL-3 and sCD23 in EK-sup. Furthermore, by contrast to IL-3, sCD23 secretion by EK is cortisone sensitive and highly enhanced by IL-4, suggesting distinct regulatory mechanisms for their production.

L77 ANSWER 40 OF 49 MEDLINE

92410457 Document Number: 92410457. PubMed ID: 1326791. Development and characterization of a human monoclonal **antibody** probably detecting the leukocyte differentiation antigen CD39. Ikewaki N; Takabe S; Tsuji K. (Department of Transplantation, Tokai University School of Medicine, Kanagawa, Japan.) TISSUE ANTIGENS, (1992 Apr) 39 (4) 174-81. Journal code: 0331072. ISSN: 0001-2815. Pub. country: Denmark. Language: English.

AB A human monoclonal IgM **antibody**, referred to as TU223, has been produced. The reactivity of TU223 was tested in various cells and cell lines by complement-dependent microcytotoxicity test and fluorescence-activated cell sorter analysis. The antigen defined by TU223 was expressed on Epstein-Barr virus-transformed B-cell lines and on some Burkitt's lymphoma cell lines, but was not expressed on normal T cells, B cells or erythrocytes. In addition, expression of the antigen defined by TU223 was also induced on B cells activated by Epstein-Barr virus or pokeweed mitogen, and on T cells activated by phytohemagglutinin, concanavalin A, pokeweed mitogen or recombinant interleukin-2. However, no expression of the antigen detected by TU223 was induced at all on recombinant interleukin-4-treated B cells or macrophage-like cell line U937. When the ability of TU223 and various mouse monoclonal **antibodies** to bind to human differentiation antigens was compared, interestingly, the reactivity of TU223 was found to be very similar to that of mouse monoclonal **antibody CD23** (H107), which reacts with Fc epsilon receptor II. Two-color analysis revealed that the antigen defined by TU223 is expressed on the cell surface of certain lymphoid cells expressing **CD23** antigen. However, it can be concluded that the antigen defined by TU223 is clearly distinct from Fc epsilon receptor II, based on assay of cross-**blocking** between H107 and TU223. The surface antigen on B85 cells recognized by TU2232 had the molecular size of 80-82 kiloDaltons as determined by immunoblotting analysis.(ABSTRACT TRUNCATED AT 250 WORDS)

L77 ANSWER 41 OF 49 SCISEARCH COPYRIGHT 2003 ISI (R)

91:565320 The Genuine Article (R) Number: GJ565. CHARACTERIZATION OF NEW RAT ANTI-MOUSE IGE MONOCLONALS AND THEIR USE ALONG WITH CHIMERIC IGE TO FURTHER DEFINE THE SITE THAT INTERACTS WITH FC-EPSILON-RII AND FC-EPSILON-RI. KEEGAN A D; FRATAZZI C; SHOPES B; BAIRD B; CONRAD D H (Reprint). DEPT MICROBIOL & IMMUNOL, BOX 678, MCV STN, RICHMOND, VA, 23298; STANFORD UNIV, DEPT CELL BIOL, STANFORD, CA, 94305; JOHNS HOPKINS UNIV, GOOD SAMARITAN HOSP, DEPT MED, DIV MOLEC RHEUMATOL, BALTIMORE, MD, 21239; BECTON DICKERSON RES CTR, MT VIEW, CA, 94039; CORNELL UNIV, DEPT CHEM, ITHACA, NY, 14853. MOLECULAR IMMUNOLOGY (1991) Vol. 28, No. 10, pp. 1149-1154. Pub. country: USA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Three rat monoclonal **antibodies** specific for mouse IgE (C12B9, 23G3, and B1E3) were established by using monoclonal anti-DNP mouse IgE (mIgE) as immunogen. These **antibodies**, as well as a fourth, (R1E4) were characterized. It was found that one **antibody** (C12B9) recognizes an allotypic determinant (Igh-7a) found on the C-epsilon chain of mIgE. **Antibody** cross-**blocking** studies and epitope mapping studies using recombinant mIgE indicated that 3 **antibodies** (C12B9, R1E4 and 23G3) were directed against the

C-epsilon-3 domain while one (B1E3) was directed against the C-epsilon-4 domain. A highly specific sandwich RIA for mIgE was developed using these **antibodies**. Use of these monoclonal anti-mIgE **antibodies** in conjunction with recombinant chimeric mIgE-human IgG1 molecules, demonstrated that the C-epsilon-3 domain is important in the binding of mIgE to the murine B cell Fc-epsilon-RII as well as to the murine mast cell Fc-epsilon-RI. The presence of the C-epsilon-4 domain influenced the binding of the recombinant IgE to the Fc-epsilon-RII; in contrast to the C-epsilon-4 domain had no effect on binding to the Fc-epsilon-RI.

L77 ANSWER 42 OF 49 CAPLUS COPYRIGHT 2003 ACS

1991:581023 Document No. 115:181023 Induction of intracellular calcium mobilization and cytotoxicity by hybrid mouse monoclonal **antibodies**. Fc.gamma.RII regulation of Fc.gamma.RI-triggered functions or signaling?. Koolwijk, Pieter; Van de Winkel, Jan G. J.; Pfefferkorn, Lorraine C.; Jacobs, Cor W. M.; Otten, Isabelle; Spierenburg, Gerrit T.; Bast, Bert J. E. G. (Dep. Mol. Biol. Biotechnol., Univ. Utrecht, Utrecht, Neth.). Journal of Immunology, 147(2), 595-602 (English) 1991. CODEN: JOIMA3. ISSN: 0022-1767.

AB The interaction was studied of bispecific mouse mAb with human IgG Fc receptors, and their ability was assessed to activate the monocytic cell line U937. Binding of monomeric hybrid anti-HuIgA1/HRP (horseradish peroxidase) mAb to the high-affinity IgG receptor, Fc.gamma.RI, on U937 cells was only obsd. when mAb with one or more mIgG2a H chains (hybrid mIgG1-2a, mIgG2a-2b, and mIgG2a-2a) were used. These Fc.gamma.RI-bound hybrid mAb were capable of enhancing the internal free cytosolic Ca2+ concn. ([Ca2+]i) in U937 cells only when bound mIgG was cross-linked using F(ab')2 fragments of goat anti-mIg **antibody**. A similar increase in [Ca2+]i was obsd. when Fc.gamma.R-bound hybrid mIgG1-2a mAb were cross-linked using goat anti-mIgG1 **antibody**, showing that the hybrid mAb themselves mediate the induction of Ca2+ increase. Remarkably, anti-Fc.gamma.RII mAb IV.3 was able to inhibit the Ca2+ increase induced via mIgG2a-1 or mIgG1-2a hybrid mAb completely, despite the fact that no effect of IV.3 on binding of monomeric hybrid mIgG1-2a or mIgG2a-1 mAb to U937 was detd. The hybrid mAb also induced lysis of HuIgA1-coated E using U937 effector cells. This lysis was completely inhibited by preincubation of U937 cells with mIgG2a mAb TB-3, which blocks Fc.gamma.RI via its Fc-part (Kurlander phenomenon). In contrast, Fc.gamma.RII-**blocking** mAb IV.3 and CIKM5 caused a significant enhancement of the **antibody**-dependent cellular cytotoxicity (ADCC) activity mediated by hybrid mIgG1-2a and mIgG2a-2b mAb. This enhancement did not occur when the parental anti-HuIgA1/2a or the hybrid anti-HuIgA1/HRP/2a-2a mAb were evaluated for ADCC activity. These findings suggest that hybrid mAb not only can bind to Fc.gamma.RI, but can mediate functional activation of myeloid cells. Given the effect of mAb IV.3 on [Ca2+]i changes and ADCC triggered through IgG1-2a mAb, Fc.gamma.RII may have a role in the regulation of Fc.gamma.RI-triggered functions or signaling.

L77 ANSWER 43 OF 49 MEDLINE

91071285 Document Number: 91071285. PubMed ID: 2147649. Functional implication for the topographical relationship between MHC class II and the low-affinity IgE receptor: occupancy of **CD23** prevents B lymphocytes from stimulating allogeneic mixed lymphocyte responses. Flores-Romo L; Johnson G D; Ghaderi A A; Stanworth D R; Veronesi A; Gordon J. (Department of Immunology, Medical School, Birmingham, GB.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1990 Nov) 20 (11) 2465-9. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Following the observation of Bonnefoy et al. (J. Exp. Med. 1988. 167:57), that the low-affinity IgE receptor (**CD23**) on B lymphocytes can be coupled (with the use of chemical cross-linking reagents) to major histocompatibility complex (MHC) class II DR molecules, we now report that ligands binding within the lectin-homology region of

CD23 prevent B cells from stimulating allogeneic mixed lymphocyte responses. Ligands capable of **blocking** mixed lymphocyte responses include the anti-**CD23 antibodies** MHM6 and EBVCS 4 but not EBVCS 1 and 5. IgE itself, and small peptides representing sequences within the CH3 domain of IgE. The detailed topographical relationship between **CD23** and MHC class II on the B lymphocyte surface was examined using dual immuno-fluorescence labeling of cells and direct visualization of the staining by confocal laser scanning microscopy. On transformed B lymphoblasts, the two antigens were seen to co-localize in discrete patches; on normal B cells which had been cultured for 2 days with interleukin 4, **CD23** and MHC class II converged at a single pole which exhibited a tendency to pseudopod formation and provided a focus for homotypic cell-cell interactions. The possibility that **CD23** could serve as a co-stimulatory-adhesion molecule in antigen presentation by B lymphocytes is discussed with special reference to a potential role in the regulation of IgE synthesis.

L77 ANSWER 44 OF 49 MEDLINE

90353389 Document Number: 90353389. PubMed ID: 2167225. IgE-dependent antigen focusing by human B lymphocytes is mediated by the low-affinity receptor for IgE. Pirron U; Schlunck T; Prinz J C; Rieber E P. (Institute for Immunology, University of Munich, FRG.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1990 Jul) 20 (7) 1547-51. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB In this study we investigated the role of the low-affinity receptor for IgE (Fc epsilon RII, **CD23**) on Epstein-Barr virus (EBV)-transformed human B cells in the uptake and presentation to T cells of antigen after complexing with IgE. Cloned EBV-transformed B cells were incubated for 5 h with (4-hydroxy-3-iodo-5-nitrophenyl)acetyl (NIP)-haptenized tetanus toxoid (NIP-TT) or NIP-TT complexed with a chimeric human IgE/mouse anti-NIP monoclonal **antibody** (IgE x NIP-TT) and then contacted for 2 min with autologous cloned TT-specific T cells. Intracellular Ca2+ mobilization in T cells was determined as an early indicator of T cell activation. The antigen-presenting capacity of B cells was significantly increased by complexing the antigen with IgE. This effect could be selectively reversed in a dose-dependent manner by **blocking** the Fc epsilon RII with an anti-**CD23** monoclonal **antibody**. The IgE-mediated increased capacity for presenting antigen became particularly evident when B cells were incubated with NIP-TT or IgE x NIP-TT for only 1 h at 4 degrees C, washed and then cultivated for 6 h at 37 degrees C allowing uptake and processing of the antigen. These results indicate a new role of the Fc epsilon RII/ **CD23** molecules in the uptake of antigen by APC which might be of importance in the maintenance of an ongoing immune response against allergens.

L77 ANSWER 45 OF 49 MEDLINE

90017517 Document Number: 90017517. PubMed ID: 2529541. Low-affinity IgE receptor (**CD23**) function on mouse B cells: role in IgE-dependent antigen focusing. Kehry M R; Yamashita L C. (Department of Immunology, DNAX Research Institute of Molecular and Cellular Biology, Inc., Palo Alto, CA 94304-1104.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Oct) 86 (19) 7556-60. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB B-cell surface immunoglobulin very efficiently focuses specific protein antigens for presentation to T cells. We have demonstrated a similar role in antigen focusing for the low-affinity Fc epsilon receptor (Fc epsilon RII) on mouse B lymphocytes. B cells treated with an IgE monoclonal **antibody** to 2,4,6-trinitrophenyl (TNP) (IgE-B cells) were 100-fold more effective than were untreated B cells in presenting low concentrations of TNP-antigen to T cells. **Blocking** the binding of IgE to Fc epsilon RII on IgE-B cells with a monoclonal **antibody**

to Fc epsilon RII completely eliminated this increased effectiveness. Preformed complexes of IgE anti-TNP and TNP-antigen were more effectively presented (approximately 100-fold) than TNP-antigen in the presence of nonspecific IgE. In contrast, complexes of IgG1 anti-TNP and TNP-antigen, capable of binding to Fc gamma receptors on B cells, were presented less effectively than TNP-antigen in the presence of nonspecific IgG1. Antigens focused by means of Fc epsilon RII or by means of B-cell surface immunoglobulin receptors were presented at comparably low concentrations. For several reasons, Fc epsilon RII on B lymphocytes seems to be particularly effective in efficiently focusing IgE-antigen complexes.

L77 ANSWER 46 OF 49 MEDLINE

89312784 Document Number: 89312784. PubMed ID: 2787453. Functional and molecular characterization of B cell line derived interleukin-1 alpha. Vyth-Dreese F A; Hekman A; Wijffels J; Geertsma M; Dellemijn T A; Dosda J; Melief C J; Bertoglio J. (Division of Immunology, The Netherlands Cancer Institute, Amsterdam.) LEUKEMIA, (1989 Aug) 3 (8) 585-92. Journal code: 8704895. ISSN: 0887-6924. Pub. country: United States. Language: English.

AB The cytokine secreted by a human hybrid B cell line (STS 25) obtained by fusion of the B lymphoblastoid cell line WI-L2-729-HF2 with neoplastic B cells from a patient with B cell non-Hodgkin's lymphoma (B-NHL) was characterized as IL-1 alpha. STS 25 cells express the idiotypic (Id+) immunoglobulin (Ig) specific for the neoplastic B cells of the B-NHL patient. STS 25 cells are weakly positive for surface mu delta kappa and in addition express the surface markers CD19, CD20, **CD23**, HLA class I and II, and the 4F2 activation antigen. STS 25 cells are also Epstein-Barr nuclear antigen positive but do not secrete viral particles. Serum-free culture supernatant from STS 25 cells (STS 25 SUP) does not show activity in assays for interleukin-2 (IL-2), -4 (IL-4), -6 (IL-6), interferon or tumor necrosis factor, but is active in the thymocyte costimulation assay and the D10.G4.1 T helper clone proliferation assay for interleukin-1 (IL-1). The IL-1 character of the STS 25 SUP activity was confirmed in inhibition studies with three different poly- or monoclonal anti-IL-1 **antibodies** (31, 88, and 94% inhibition in thymocyte costimulation assay, respectively). Furthermore, complete **blocking** of D10.G4.1 cell proliferation mediated by STS 25 SUP was observed by including anti-IL-1 alpha specific **antibody** in the assay, whereas anti-IL-1 beta **antibody** had no effect. These results indicate that this STS 25 SUP activity can be attributed to the presence of IL-1 alpha in the supernatant. Northern blot analysis of total STS 25 cellular RNA using IL-1 alpha or IL-1 beta specific probes revealed the constitutive expression of IL-1 alpha messenger RNA by STS 25 cells. In contrast, no IL-1 beta message was detectable, not even after treatment of the cells with phorbol ester or cycloheximide, which resulted in approximately 5-fold enhancement of IL-1 alpha mRNA expression. Binding studies with radiolabeled recombinant (r) IL-1 alpha indicated the presence of high numbers of IL-1 receptors on STS 25 cells (1,170 per cell, Kd = 392 pM). Although both IL-1 alpha and IL-1 beta bound to these IL-1 receptors, no indication was found for IL-1 mediated regulation of STS 25 cell growth.(ABSTRACT TRUNCATED AT 400 WORDS)

L77 ANSWER 47 OF 49 MEDLINE

90162835 Document Number: 90162835. PubMed ID: 2623739. B- and T-cell activation in the thymus of patients with myasthenia gravis. Cohen-Kaminsky S; Leprince C; Galanaud P; Richards Y; Berrih-Aknin S. (CNRS URA-D1159, Centre Chirurgical Marie Lannelongue, Le Plessis-Robinson, France.) THYMUS, (1989) 14 (1-3) 187-93. Journal code: 8009032. ISSN: 0165-6090. Pub. country: Netherlands. Language: English.

AB The activation state of thymic T and B lymphocytes was phenotypically and functionally explored in patients with Myasthenia Gravis (MG). We detected no phenotypic signs of activation in fresh total thymic lymphocyte suspensions (CD25 expression) while functional signs of activation were reflected by a significantly higher sensitivity to

recombinant IL-2 (rIL-2) without any previous stimulation in MG patients as compared to controls. The response to rIL-2 was time-and dose-dependent, was inhibited by a **blocking** anti-IL-2 receptor **antibody**, and was associated to an increase of CD25+ T cells. Thymic B-cell populations purified after T cell and macrophage depletion, expressed at variable levels activation markers such as the transferrin receptor, the CD25, 4F2, **CD23** and B8.7 Ag, indicating that a marked proportion of them are activated. Moreover, these B-cell populations were spontaneously sensitive to BCGF-12-kD and to a lesser extent to rIL-2, demonstrating that they also exhibit functional signs of activation. The largest proportion of activated B cells and the most intense response to BCGF-12-kD was found in patients presenting the highest anti-acetylcholine receptor (AChR) titers. Our data confirm the hyperactivity of the thymus gland in MG, reflected by the presence of T and B cells with functional signs of pre-activation. These cells could conceivably be located in lymphoid follicles and may represent autoreactive cells involved in the autoimmune process. Whether they are sensitized to AChR remains to be investigated.

L77 ANSWER 48 OF 49 MEDLINE

89053411 Document Number: 89053411. PubMed ID: 2461344. Characterization of two **CD23** monoclonal **antibodies** with reactivity distinct from other **antibodies** within this cluster of differentiation. Goff L K; Armitage R J; Beverley P C. (Imperial Cancer Research Fund, Human Tumour Immunology Group, London, U.K.) IMMUNOLOGY, (1988 Oct) 65 (2) 213-20. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB We have produced two **CD23** monoclonal **antibodies** (mAb), LA1 and LA2, which differ significantly in their patterns of reactivity compared to other mAb within this cluster. Unlike other **CD23** mAb, LA1 and LA2 show virtually no reactivity with freshly isolated tonsil B lymphocytes or mantle zone lymphocytes in tissue section. That LA1 and LA2 are **CD23** mAb is confirmed by their precipitation of a 45,000 MW surface protein from B cells and strong reactivity with a **CD23** transfectant. Cross-**blocking** studies with four well-characterized **CD23** mAb show that LA1 and LA2 recognize the same, distinct epitope of the **CD23** molecule. However, similar to other **CD23** mAb, expression of LA1 and LA2 increases after activation. Following removal of cells staining with the well-characterized **CD23** mAb MHM6, using a highly efficient magnetic bead technique, LA1 and LA2, but not other **CD23** mAb, react with a subpopulation of the remaining cells when activated with interleukin-4 (IL-4) or phorbol ester. Soluble LA1 and MHM6 both provide a co-stimulatory signal for phorbol ester-induced B-cell proliferation. This response is increased if these mAb are used to cross-link the **CD23** molecule. Interestingly, despite the fact that LA2 and LA1 cross-block, LA2 has no effect on functional responses in its soluble form but can elicit a comparable increase in proliferation when cross-linked. Results presented here suggest that the novel **CD23** mAb, LA1 and LA2, recognize a distinct form of the **CD23** molecule, expressed only on activation. These mAb define a subpopulation of activated B cells which do not stain with other **CD23** mAb.

L77 ANSWER 49 OF 49 CAPLUS COPYRIGHT 2003 ACS

1988:148489 Document No. 108:148489 Signals involved in T cell activation. T cell proliferation induced through the synergistic action of anti-CD28 and anti-CD2 monoclonal **antibodies**. Van Lier, Rene A. W.; Brouwer, Miranda; Aarden, Lucien A. (Cent. Lab. Netherlands Red Cross Blood Transfus. Serv., Univ. Amsterdam, Amsterdam, Neth.). European Journal of Immunology, 18(1), 167-72 (English) 1988. CODEN: EJIMAF. ISSN: 0014-2980.

AB Monoclonal **antibodies** (mAb) directed against the T cell differentiation antigen **CD23** (Tp44) induce proliferation of

resting T lymphocytes in the presence of phorbol esters. Moreover, such **antibodies** augment and sustain T cell proliferation induced by sol. antigens, phytohemagglutinin, and anti-CD3 mAb. In monocyte-depleted T cell suspensions, anti-CD28 mAb 9.3 and Kolt-2 were able to circumvent the requirement for interleukin 2 (IL2) in T cell proliferation induced by sol. anti-CD3 **antibodies**. Apart from the synergy of anti-CD28 **antibodies** with phorbol myristate acetate and anti-CD3 **antibodies**, anti-CD28 mAb were able to induce T cell mitogenesis in combination with an erythrocyte rosette-**blocking** anti-CD2 **antibody**. **Antibodies** directed against different epitopes on the CD2 antigen can synergize with anti-CD28 mAb. Proliferation induced through the synergistic action of anti-CD28 mAb with anti-CD2 **antibodies** can be induced in the absence of accessory cells and is accompanied by the prodn. of IL2 and the expression of IL2 receptors. Detectable Ca2+ mobilization was not induced through the simultaneous binding of anti-CD28 and anti-CD2 mAb. Thus, IL2-dependent proliferation can be induced through the simultaneous binding of anti-CD28 and anti-CD2 **antibodies**, possibly through phosphatidylinositol-independent pathways.

=> s (bonnefoy j?/au or Crowe J?/au or Ware J?/au or Rapson n?/au or Shearin J?/au)
L78 7188 (BONNEFOY J?/AU OR CROWE J?/AU OR WARE J?/AU OR RAPSON N?/AU OR SHEARIN J?/AU)

=> s l78 and CD23 antibody
L79 12 L78 AND CD23 ANTIBODY

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PROCESSING COMPLETED FOR L79
L80 7 DUP REMOVE L79 (5 DUPLICATES REMOVED)

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L80 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS
1999:736930 Document No. 131:350265 Antibodies to CD23. **Bonnefoy, Jean-Yves Marcel Paul**; Crowe, Scott James; Ellis, Jonathan Henry; **Rapson, Nicholas Timothy**; **Shearin, Jean** (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.
AB The authors disclose the prepn. and characterization of murine monoclonal and humanized antibodies which bind to the CD23 (Fc.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to CD23 with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these antibodies may find use in the treatment of autoimmune and inflammatory disorders.

L80 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1999:1848 Document No.: PREV199900001848. Binding of anti-CD23 monoclonal antibody to the leucine zipper motif of FcepsilonRII/CD23 on B cell membrane promotes its proteolytic cleavage. Evidence for an effect on the oligomer/monomer equilibrium. Munoz, Olivier; Brignone, Chrystelle; Grenier-Brossette, Nicole; **Bonnefoy, Jean-Yves**; Cousin, Jean-Louis (1). (1) INSERM U343, Hopital de l'Archet, B.P. 79, F-06202. Nice cedex 03 France. Journal of Biological Chemistry, (Nov. 27, 1998)

Vol. 273, No. 48, pp. 31795-31800. ISSN: 0021-9258. Language: English.

AB In the present study we have compared the binding of two monoclonal antibodies to CD23, EBVCS1 and mAb25, which recognize the stalk and the lectin domain, respectively, on the CD23 molecule. At 4degreeC, EBVCS1 binds to about 10% of the receptors recognized by mAb25 on the B cell surface. At 37degreeC, whereas mAb25 reaches its maximal binding within a few seconds, EBVCS1 requires 60 min to bind to the same extent. Stabilization of the oligomeric structure of CD23 with IgE strongly affects in a dose-dependent fashion the number of binding sites seen by EBVCS1 but not the t1/2 to reach them, suggesting that EBVCS1 binds to the coiled coil region through an allosteric mechanism. EBVCS1 rapidly down-modulates the membrane CD23 expression with a coincident increase of CD23-soluble fragments in the culture medium, an effect that is inhibited by IgE. In contrast, mAb25, as well as IgE, protects CD23 from proteolytic cleavage and stimulates its endocytosis. These results suggest that EBVCS1 unravels the coiled coil structure of CD23, rendering it more susceptible to proteolytic attack. This supports the oligomeric model proposed previously (Gould, H., Sutton, B., Edmeades, R., and Beavil, A. (1991) Monogr. Allergy 29, 28-49). The biological significance of these observations is discussed.

L80 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

1999:124107 Document No.: PREV199900124107. CD23 modulates leukotriene-mediated broncho-constriction in a murine model of allergic asthma. Dasic, Gorana (1); Juillard, Pierre (1); Graber, Pierre (1); Herren, Suzanne (1); Angell, Tony; Knowles, Richard; **Bonnefoy, Jean-Yves**; Kosco-Vilbois, Marie H. (1); Chvatchko, Yolande (1). (1) Geneva Biomed. Res. Inst., Glaxo Wellcome Res. and Dev. S.A., CH-1228 Plan-les-Ouates, Geneva Switzerland. European Respiratory Journal, (Sept., 1998) Vol. 12, No. SUPPL. 28, pp. 193S. Meeting Info.: European Respiratory Society Annual Congress Geneva, Switzerland September 19-23, 1998 The European Respiratory Society. ISSN: 0903-1936. Language: English.

L80 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS

1996:380155 Document No. 125:31943 Binding agents to CD23. **Bonnefoy, Jean-Yves Marcel Paul** (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD23 useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized antibody or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23 antibody**, CD23-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal antibodies decrease CD23-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant CD23 to CD11b and CD11c, etc.

L80 ANSWER 5 OF 7 MEDLINE DUPLICATE 1

96071560 Document Number: 96071560. PubMed ID: 7585180. Marked amelioration of established collagen-induced arthritis by treatment with antibodies to CD23 in vivo. Plater-Zyberk C; **Bonnefoy J Y.** (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland.) NATURE MEDICINE, (1995 Aug) 1 (8) 781-5. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB CD23 is a low-affinity receptor for immunoglobulin E (IgE) expressed by a

variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. CD23 regulates many functional aspects of immune cells, both in its cell-associated and soluble forms. In view of the increased levels of CD23 in rheumatoid arthritis, we have studied the effect of neutralizing CD23 in type II collagen-induced arthritis in mice, a model for human rheumatoid arthritis. Successful disease modulation is achieved by treatment of arthritic DBA/1 mice with either polyclonal or monoclonal antibodies to mouse CD23. Treated mice show a dose-related amelioration of arthritis with significantly reduced clinical scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decrease in cellular infiltration of the synovial sublining layer and limited destruction of cartilage and bone is evident in animals treated with therapeutic doses of anti-**CD23 antibody**. These findings demonstrate the involvement of CD23 in a mouse model of human rheumatoid arthritis.

L80 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1995:521449 Document No.: PREV199598535749. Treatment with antibodies to CD23 markedly ameliorates an established collagen-induced arthritis in mice. Plater-Zyberk, Christine; **Bonnefoy, Jean-Yves**. Glaxo IMB, Immunol. Dep., 14 Chemin Des Aulx, CH-1228 Geneva Switzerland. Arthritis & Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S310. Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals San Francisco, California, USA October 21-26, 1995 ISSN: 0004-3591. Language: English.

L80 ANSWER 7 OF 7 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 2
91:364397 The Genuine Article (R) Number: FT273. IGE AND SWITCHING PHENOMENA. **BONNEFOY J Y (Reprint)**. GLAXO INST MOLEC BIOL, CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND (Reprint). SEMAINE DES HOPITAUX (1991) Vol. 67, No. 26-2, pp. 1199-1200. Pub. country: SWITZERLAND. Language: French.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In allergic disorders, IgE increases following allergen stimulation. In vitro IgE synthesis is the result of a complex interaction between T-cells, B-cells and monocytes, controlled by cytokines produced by T-cells and monocytes (IL-4, IL-5, IFN-gamma, and IL-6). IL-4 acts as a switching factor to induce synthesis of IgE. IFN-gamma inhibits IL-4 induced IgE synthesis. IL-4 is a mastocyte growth factor, as well as IL-3. Moreover, IL-4 is a potent inducer of FceR/CD23 expression of B-cells and monocytes. Monoclonal anti-**CD23 antibodies** inhibit IL-4-induced IgE synthesis in an isotype-specific manner. IL-4-producing T-cells also produce IL-5 which induces differentiation of eosinophil precursors. Eosinophils, in turn, express low affinity receptors for IgE when activated. Activation of the IgE system thus leads to increased IgE production and increased expression of IgE receptors. This results in increased receptor-ligand interactions, resulting in release of numerous chemical mediators involved in the pathogenesis of allergic disorders.

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:30:38 ON 23 APR 2003
L1 2419928 S ANTIBODY
L2 3300 S L1 AND CD23
L3 90 S L2 AND CHIMERIC

L4	9	S L3 AND HUMANIZED
L5	9	DUP REMOVE L4 (0 DUPLICATES REMOVED)
L6	0	S L3 AND BINDING AFFINITY
L7	6	S L2 AND BINDING AFFINITY
L8	6	DUP REMOVE L7 (0 DUPLICATES REMOVED)
L9	218	S ANTIBODY BINDING AFFINITY
L10	0	S L9 AND ANTI-CD23
L11	0	S L9 AND CD23
L12	0	S L9 AND FC EPSILON RECEPTOR II
L13	0	S L9 AND "RSSKSLLYKDGKTYLN"
L14	0	S L9 AND "1X109 KA PER M"
L15	0	S L2 AND BIOCORE ASSAYS
L16	0	S L2 AND BIACORE ASSAY
L17	111	DUP REMOVE L9 (107 DUPLICATES REMOVED)
L18	0	S L17 AND CD23 ANTIBODY
L19	88	S L2 AND ANTAGONIST
L20	59	DUP REMOVE L19 (29 DUPLICATES REMOVED)
L21	0	S L2 AND "CLONE C11"
L22	38	DUP REMOVE L3 (52 DUPLICATES REMOVED)
L23	1353	DUP REMOVE L2 (1947 DUPLICATES REMOVED)
L24	31	S L23 AND ARTHRITIS
L25	31	DUP REMOVE L24 (0 DUPLICATES REMOVED)
L26	25	S L23 AND LUPUS ERYTHEMATOSUS
L27	25	DUP REMOVE L26 (0 DUPLICATES REMOVED)
L28	192	S L23 AND TREATMENT
L29	8	S L28 AND ARTHRITIS
L30	8	DUP REMOVE L29 (0 DUPLICATES REMOVED)
L31	7	S L28 AND LUPUS ERYTHEMATOSUS
L32	7	DUP REMOVE L31 (0 DUPLICATES REMOVED)
L33	0	S L28 AND HASHIMOTOS THYROIDITIS
L34	5	S L28 AND MULTIPLE SCLEROSIS
L35	5	DUP REMOVE L34 (0 DUPLICATES REMOVED)
L36	3	S L28 AND DIABETES
L37	3	DUP REMOVE L36 (0 DUPLICATES REMOVED)
L38	4	S L28 AND UVEITIS
L39	4	DUP REMOVE L38 (0 DUPLICATES REMOVED)
L40	16	S L28 AND DERMATITIS
L41	16	DUP REMOVE L40 (0 DUPLICATES REMOVED)
L42	4	S L28 AND PSORIASIS
L43	4	DUP REMOVE L42 (0 DUPLICATES REMOVED)
L44	4	S L28 AND URTICARIA
L45	4	DUP REMOVE L44 (0 DUPLICATES REMOVED)
L46	3	S L28 AND NEPHROTIC SYNDROME
L47	3	DUP REMOVE L46 (0 DUPLICATES REMOVED)
L48	5	S L28 AND GLOMERULONEPHRITIS
L49	5	DUP REMOVE L48 (0 DUPLICATES REMOVED)
L50	0	S L28 AND INFLAMMATORY BOWEL DISEASE
L51	4	S L28 AND ULCERATIVE COLITIS
L52	4	DUP REMOVE L51 (0 DUPLICATES REMOVED)
L53	0	S L28 AND "CROHN'S DISASE"
L54	0	S L28 AND SJOGRENS SYNDROME
L55	3	S L28 AND ALLERGIES
L56	3	DUP REMOVE L55 (0 DUPLICATES REMOVED)
L57	23	S L28 AND ASTHMA
L58	23	DUP REMOVE L57 (0 DUPLICATES REMOVED)
L59	15	S L28 AND RHINITIS
L60	15	DUP REMOVE L59 (0 DUPLICATES REMOVED)
L61	11	S L28 AND ECZEMA
L62	11	DUP REMOVE L61 (0 DUPLICATES REMOVED)
L63	0	S L28 AND GRAFT VERSUS HOST
L64	0	S L28 AND GVH
L65	1	S L28 AND COPD
L66	3	S L28 AND INSULITIS

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L67            3 DUP REMOVE L66 (0 DUPLICATES REMOVED)
L68            4 S L28 AND BRONCHITIS
L69            4 DUP REMOVE L68 (0 DUPLICATES REMOVED)
L70            0 S L28 AND TYPE I DIABETES
L71            3 S L28 AND B CELL MALIGNANCIES
L72            3 DUP REMOVE L71 (0 DUPLICATES REMOVED)
L73            0 S L28 AND BLOCK SOLUBLE CD23 FORMATION
L74           49 S L23 AND BLOCKING
L75            3 S L74 AND SOLUBLE CD23
L76            3 DUP REMOVE L75 (0 DUPLICATES REMOVED)
L77           49 DUP REMOVE L74 (0 DUPLICATES REMOVED)
L78         7188 S (BONNEFOY J?/AU OR CROWE J?/AU OR WARE J?/AU OR RAPSON N?/AU
L79           12 S L78 AND CD23 ANTIBODY
L80            7 DUP REMOVE L79 (5 DUPLICATES REMOVED)

=> s l78 and antibody
L81          947 L78 AND ANTIBODY

=> s l81 and CD23
L82          185 L81 AND CD23

=> s l82 and affinity
L83          106 L82 AND AFFINITY

=> dup remove l83
PROCESSING COMPLETED FOR L83
L84           36 DUP REMOVE L83 (70 DUPLICATES REMOVED)

=> d l84 1-36 cbib abs

L84  ANSWER 1 OF 36      MEDLINE                              DUPLICATE 1
1999438051  Document Number: 99438051.    PubMed ID: 10508270.   Critical role
      of CD23 in allergen-induced bronchoconstriction in a murine
      model of allergic asthma. Dasic G; Juillard P; Graber P; Herren S; Angell
      T; Knowles R; Bonnefoy J Y; Kosco-Vilbois M H; Chvatchko Y.
      (Department of Immunology Geneva Biomedical Research Institute, Glaxo
      Wellcome Research and Development S.A., Geneva, Switzerland. ) EUROPEAN
      JOURNAL OF IMMUNOLOGY, (1999 Sep) 29 (9) 2957-67.  Journal code: 1273201.
      ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of.
      Language: English.
AB    CD23-deficient and anti-CD23 monoclonal
      antibody-treated mice were used to investigate the role of the
      low-affinity receptor for IgE (CD23) in allergic
      airway inflammation and airway hyperresponsiveness (AHR).  While there
      were no significant differences in ovalbumin (OVA)-specific IgE titers and
      tissue eosinophilia, evaluation of lung function demonstrated that
      CD23-/- mice showed an increased AHR to methacholine (MCh) when
      compared to wild-type mice but were completely resistant to the OVA
      challenge.  Anti-CD23 Fab fragment treatment of wild-type mice
      did not affect the MCh-induced AHR but significantly reduced the
      OVA-induced airway constriction.  These results imply a novel role for
      CD23 in lung inflammation and suggest that anti-CD23 Fab
      fragment treatment may be of therapeutic use in allergic asthma.

L84  ANSWER 2 OF 36  EMBASE  COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 2
1999134306  EMBASE  Binding of anti-CD23 monoclonal antibody
      to the leucine zipper motif of Fc.epsilon.RII/CD23 on B cell
      membrane promotes its proteolytic cleavage: Evidence for an effect on the
      oligomer/monomer equilibrium. Munoz O.; Brignone C.; Grenier-Brossette N.;
      Bonnefoy J.-Y.; Cousin J.-L.. J.-L. Cousin, INSERM U343, Hopital
      de l'Archet, BP 79, F-06202 Nice Cedex 03, France. cousin@unice.fr.
      Journal of Biological Chemistry  273/48 (31795-31800)  27 Nov 1999.
      Refs: 54.
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ISSN: 0021-9258. CODEN: JBCHA3. Pub. Country: United States. Language: English. Summary Language: English.

AB In the present study we have compared the binding of two monoclonal **antibodies** to **CD23**, EBVCS1 and mAb25, which recognize the stalk and the lectin domain, respectively, on the **CD23** molecule. At 4.degree.C, EBVCS1 binds to about 10% of the receptors recognized by mAb25 on the B cell surface. At 37.degree.C, whereas mAb25 reaches its maximal binding within a few seconds, EBVCS1 requires 60 min to bind to the same extent. Stabilization of the oligomeric structure of **CD23** with IgE strongly affects in a dose-dependent fashion the number of binding sites seen by EBVCS1 but not the t(1/2) to reach them, suggesting that EBVCS1 binds to the coiled coil region through an allosteric mechanism. EBVCS1 rapidly down-modulates the membrane **CD23** expression with a coincident increase of **CD23** -soluble fragments in the culture medium, an effect that is inhibited by IgE. In contrast, mAb25, as well as IgE, protects **CD23** from proteolytic cleavage and stimulates its endocytosis. These results suggest that EBVCS1 unravels the coiled coil structure of **CD23**, rendering it more susceptible to pro, teolytic attack. This supports the oligomeric model proposed previously (Gould, H., Sutton, B., Edmeades, R., and Beavil, A. (1991) Monogr. Allergy 29, 28-49). The biological significance of these observations is discussed.

L84 ANSWER 3 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)

1998:809537 The Genuine Article (R) Number: 129JL. Soluble CD21 (sCD21) forms biologically active complexes with **CD23**: sCD21 is present in normal plasma as a complex with trimeric **CD23** and inhibits soluble **CD23**-induced IgE synthesis by B cells. FremeauxBacchi V; Fischer E; LecoanetHenchoz S; Mani J C; **Bonnefoy J Y**; Kazatchkine M D (Reprint). HOP BROUSSAIS, INSERM, U430, 96 RUE DIDOT, F-75014 PARIS, FRANCE (Reprint); HOP BROUSSAIS, INSERM, U430, F-75014 PARIS, FRANCE; GLAXO INST MOL BIOL SA, CH-1228 GENEVA, SWITZERLAND; CNRS, UMR 9921, F-34060 MONTPELLIER, FRANCE. INTERNATIONAL IMMUNOLOGY (OCT 1998) Vol. 10, No. 10, pp. 1459-1466. Publisher: OXFORD UNIV PRESS. GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND. ISSN: 0953-8178. Pub. country: FRANCE; SWITZERLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A soluble form of CD21 (sCD21) of 135 kDa is spontaneously released by human B and T lymphocytes upon shedding of the extracellular domain of the molecule. By Western blotting, we have now identified two forms of sCD21 of M-r 135 and 90 kDa in normal human serum. We further demonstrate that sCD21 circulates in a complexed form with cleavage fragments of C3 and **CD23**, two previously identified ligands of the membrane CD21 receptor. The **CD23** molecule was in the form of a trimer in the soluble complex purified from plasma by **affinity** chromatography on anti-CD21 Sepharose. The serum sCD21 complex was also found to contain IgE, The presence of IgE and of CD21 in a soluble complex that contains trimeric **CD23** as the only form of soluble **CD23** (sCD23) is in agreement with a model in which two of the three lectin heads of **CD23** bind to the C(epsilon)3 domain of IgE, thus leaving one of the heads available for interaction with CD21. We further demonstrate that sCD21 inhibits sCD23-induced IgE synthesis by IL-4-stimulated B cells. The results indicate that sCD21 in plasma retains the ligand-binding properties of the membrane CD21 receptor and exhibits immunoregulatory properties that may be relevant to allergic and inflammatory disorders.

L84 ANSWER 4 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)

97:532647 The Genuine Article (R) Number: XJ674. The 25-kDa soluble **CD23** activates type III constitutive nitric oxide-synthase activity via CD11b and CD11c expressed by human monocytes. Aubry J P (Reprint); Dugas N; LecoanetHenchoz S; Ouaaz F; Zhao H X; Delfraissy J F; Graber P; Kolb J P; Dugas B; **Bonnefoy J Y**. GLAXO WELLCOME INC, GENEVA BIOMED RES INST, DEPT IMMUNOL, 14 CHEMIN AULX, CH-1228 PLAN LES

OUATES, GENEVA, SWITZERLAND (Reprint); GLAXO WELLCOME INC, GENEVA BIOMED RES INST, DEPT IMMUNOL, CH-1228 GENEVA, SWITZERLAND; HOP KREMLIN BICETRE, LAB VIRUS NEURONE & IMMUNITE, LE KREMLIN BICETR, FRANCE; HOP LA PITIE SALPETRIERE, CNRS URA 625, PARIS, FRANCE; INST CURIE, INSERM U365, PARIS, FRANCE. JOURNAL OF IMMUNOLOGY (15 JUL 1997) Vol. 159, No. 2, pp. 614-622. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: SWITZERLAND; FRANCE. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **CD23**, a low-**affinity** receptor for IgE, was recently shown to bind to CD11b and CD11c molecules on human monocytes, The 25-kDa soluble fragment of **CD23** (sCD23), was tested for its capacity to elicit various signaling pathways in human monocytes, sCD23 was found to trigger an early increase in cGMP accumulation, through the generation of nitric oxide, This was a result of activating the L-arginine pathway, since the sCD23-mediated effect was inhibited in the presence of substituted nonmetabolizable L-arginine analogues, In addition, the increase in cGMP was suppressed by calcium chelators and inhibitors of the calcium/calmodulin complex, suggesting the involvement of a constitutive, calcium-dependent nitric oxide synthase (NOS), Indeed, the presence of an endothelial constitutive type III NOS mRNA was detected in nonactivated human monocytes, and the corresponding protein has been detected by flow cytometry, Moreover, sCD23 was shown to induce a calcium influx in monocytes, in accordance with an activation of a constitutive NOS through a transient increase in [Ca2+](i). As expected, these events were mimicked by mAbs against CD11b and CD11c, the macrophage receptors for **CD23** , In addition to these early events, sCD23 and the agonistic anti-CD11b and CD11c mAbs, which all trigger the release of proinflammatory mediators such as TNF-alpha, were shown to act through an NO-dependent process.

L84 ANSWER 5 OF 36 MEDLINE DUPLICATE 3

97351082 Document Number: 97351082. PubMed ID: 9207458. Inhibition of apoptosis in a human pre-B-cell line by **CD23** is mediated via a novel receptor. White L J; Ozanne B W; Graber P; Aubry J P; **Bonnefoy J Y**; Cushley W. (Institute of Biomedical & Life Sciences, University of Glasgow, Scotland, UK.) BLOOD, (1997 Jul 1) 90 (1) 234-43. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB Human **CD23** is a 45-kD type II membrane glycoprotein, which functions as a low-**affinity** receptor for IgE and as a ligand for the CD21 and CD11b/CD11c differentiation antigens. **CD23** is released from the surface of cells as soluble fragments, and a 25-kD species of soluble **CD23** (sCD23) appears to act as a multifunctional cytokine. In this report, sCD23 is shown to sustain the growth of low cell density cultures of a human pre-B-acute lymphocytic leukemia cell line, SMS-SB: no other cytokine tested was able to induce this effect. Flow cytometric analysis indicates that sCD23 acts to prevent apoptosis of SMS-SB cells. SMS-SB cells cultured at low cell density possess low levels of bcl-2 protein. Addition of sCD23 to cells at low cell density maintained bcl-2 expression at levels equivalent to those observed in SMS-SB cells cultured at higher cell densities. No **CD23** mRNA was found in SMS-SB cells, ruling out an autocrine function for **CD23** in this cell line model. Although SMS-SB cells do not express the known receptors for **CD23**, namely CD21, CD11b-CD18, or CD11c-CD18, the cells specifically bind **CD23** -containing liposomes, but not glycophorin-containing liposomes. Binding of **CD23**-containing liposomes is inhibited by anti-**CD23** but not by anti-CD21 or anti-CD11b/c monoclonal **antibodies**. The data show that sCD23 prevents apoptosis of the SMS-SB cell line by acting through a novel receptor.

L84 ANSWER 6 OF 36 MEDLINE DUPLICATE 4

96305405 Document Number: 96305405. PubMed ID: 8766552. Human lymphocytes

shed a soluble form of CD21 (the C3dg/Epstein-Barr virus receptor, CR2) that binds iC3b and **CD23**. Fremeaux-Bacchi V; Bernard I; Maillet F; Mani J C; Fontaine M; **Bonnefoy J Y**; Kazatchkine M D; Fischer E. (INSERM U430, Hopital Broussais, Paris, France.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jul) 26 (7) 1497-503. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB We report on a soluble (s) form of CD21 (the C3dg/Epstein-Barr virus receptor, CR2) that is spontaneously released by B and T lymphocytes. Immunoprecipitation with anti-CD21 mAb of culture supernatants of surface and biosynthetically labeled B and T cell lines revealed a single band with an apparent molecular mass of 135 kDa. The molecule exhibited a molecular mass 10 kDa lower than that of membrane CD21. The release of soluble CD21 (sCD21) was time dependent and correlated with a parallel decrease in the expression of the membrane-associated molecule. The protein was also found in culture supernatants of tonsillar B cells and normal human thymocytes. Epitopic analysis using combinations of anti-CD21 monoclonal **antibodies** (mAb) indicated that sCD21 and membrane CD21 were similarly recognized by mAb directed against short consensus repeats (SCR) 1-2, SCR 4-5 and SCR 9-11. **Affinity** -purified sCD21 was capable of binding to purified human iC3b and to human recombinant **CD23**, as assessed by enzyme-linked immunosorbent assay and by using the BIAcore technology. In addition, normal human serum was found to contain a soluble form of CD21 that exhibited a similar molecular mass to that of the molecule shed by B and T cells in culture. The serum form of CD21 was recognized by all anti-CD21 mAb that we tested and showed a high reactivity with mAb directed against SCR 1-2. Our observations suggest that B and T cells shed the extracellular portion of CD21 and release a soluble molecule that retains the ligand-binding properties of CD21, thus having a potential role in immunoregulation.

L84 ANSWER 7 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)

96:675067 The Genuine Article (R) Number: VG106. A NEW ROLE FOR **CD23** IN INFLAMMATION. **BONNEFOY J Y (Reprint)**; PLATERZYBERK C; LECOANETHENCHOZ S; GAUCHAT J F; AUBRY J P; GRABER P. IMMUNOLOGY TODAY (SEP 1996) Vol. 17, No. 9, pp. 418-420. ISSN: 0167-5699. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **CD23**, is expressed on a variety of haematopoietic cell types and displays pleiotropic activities in vitro. Here Jean-Yves Bonnefoy and collegues discuss a novel interaction between **CD23** and the alpha chains of the beta(2) integrins, CD11b and CD11c, that leads to a proinflammatory pattern of macrophage activation. They describe how neutralizing **antibodies** to **CD23** can decrease the severity of murine arthritis.

L84 ANSWER 8 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)

96:662167 The Genuine Article (R) Number: VE782. PAIRS OF SURFACE MOLECULES INVOLVED IN HUMAN IGE REGULATION - **CD23**-CD21 AND CD40-CD40L. **BONNEFOY J Y (Reprint)**; GAUCHAT J F; LIFE P; GRABER P; MAZZEI G; AUBRY J P. GLAXO INST MOL BIOL SA, DEPT IMMUNOL, 14 CHEMIN AULX, CH-1228 PLAN LES OUATES, GENEVA, SWITZERLAND (Reprint). EUROPEAN RESPIRATORY JOURNAL (AUG 1996) Vol. 9, Supp. 22, pp. S63-S66. ISSN: 0903-1936. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB At least two cell-derived signals have been shown to be necessary for the induction of immunoglobulin isotype switching in B-cells. The first signal is given by either of the soluble lymphokines, interleukin (IL)-4 or IL-13, which induce germline epsilon transcript expression, but this alone is insufficient to trigger secretion of immunoglobulin E (IgE). The second signal is provided by a physical interaction between B-cells and activated T-cells, basophils and mast cells, and it has been shown that the CD40/CD40 ligand (CD40L) pairing is crucial for mediating IgE synthesis.

In hyper-immunoglobulin M1 (HIGM1) syndrome, which is characterized by greatly decreased levels of immunoglobulin G, A and E (IgG, IgA and IgE), there are mutations in the CD40L resulting in a completely non-functional extracellular domain, The CD40L is, therefore, playing a central role in immunoglobulin isotype switching.

Amongst the numerous pairs of surface adhesion molecules, the **CD23**-CD21 pair seems to play a key role in the generation of IgE, The **CD23** molecule is positively and negatively regulated by factors which increase or decrease IgE production, respectively, **Antibodies** to **CD23** have been shown to inhibit IL-4-induced human IgE production in vitro and to inhibit antigen-specific IgE responses in a rat model, in an isotype selective manner, **CD23** interacts with CD21 on B-cells, preferentially driving IgE production. **CD23** recognizes two main epitopes on the CD21 molecule. One region consists of short consensus repeat (SCR) sequences 1-2 and the other of SCR 5-8, In the latter region, Asn 370 and 295 are critical in the interaction with the lectin **CD23**.

Therefore, a restricted number of cytokines and surface molecules seems to selectively regulate human immunoglobulin E synthesis.

L84 ANSWER 9 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)

96:369839 The Genuine Article (R) Number: UJ686. THE EPSTEIN-BARR VIRUS-BINDING SITE ON CD21 IS INVOLVED IN **CD23** BINDING AND INTERLEUKIN-4-INDUCED IGE AND IGG4 PRODUCTION BY HUMAN B-CELLS. HENCHOZLECOANET S; JEANNIN P; AUBRY J P; GRABER P; BRADSHAW C G; POCHON S; **BONNEFOY J Y (Reprint)**. GLAXO INST MOLEC BIOL, DEPT IMMUNOL, 14 CHEMIN AULX, CASE POSTALE 674, 1228 PLAN OUATES, GENEVA, SWITZERLAND (Reprint); GLAXO INST MOLEC BIOL, DEPT IMMUNOL, GENEVA, SWITZERLAND. IMMUNOLOGY (MAY 1996) Vol. 88, No. 1, pp. 35-39. ISSN: 0019-2805. Pub. country: SWITZERLAND. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human CD21 has previously been described as a receptor for the C3d,g and iC3b proteins of complement, as a receptor for the gp350/220 envelope glycoprotein of the Epstein-Barr virus (EBV) and also as a receptor for interferon-alpha (IFN-alpha). Structurally, CD21 consists of 15 to 16 short consensus repeats (SCR) of 60 to 75 amino acids followed by a transmembrane domain and an intracytoplasmic region. We reported that **CD23**, a low-**affinity** receptor for IgE (Fc epsilon R2), is a new functional ligand for CD21. We recently found that the sites of interaction of **CD23** on CD21 are on SCR 5 to 8 and 1-2. The first site is a lectin-sugar type of interaction and the second site is a protein-protein interaction. We report here that amongst the other ligands for CD21 (EBV, C3d,g and IFN-alpha), only EBV is able to inhibit the binding of **CD23** to CD21. Furthermore, even a peptide from gp350/220 of EBV known to bind to CD21 is able to decrease **CD23** binding to CD21. Since **CD23**/CD21 pairing is important in the control of IgE production, we tested the effect of the EBV-derived peptide on immunoglobulin production from peripheral blood mononuclear cells and purified tonsillar B cells. Interestingly, the EBV-peptide inhibited IgE and IgG4 production induced by interleukin-4, in a dose-dependent manner. The same results were obtained using either peripheral blood mononuclear cells or purified tonsillar B cells. Another CD21 ligand, C3, did not affect binding of **CD23** to CD21 nor the production of IgE and IgG4. This study indicates that blocking **CD23** binding to CD21 SCR 2 on human B cells selectively modulates immunoglobulin production.

L84 ANSWER 10 OF 36 MEDLINE DUPLICATE 5

95347383 Document Number: 95347383. PubMed ID: 7542593. CD20 monoclonal **antibodies** decrease interleukin-4-stimulated expression of the low-**affinity** receptor for IgE (Fc epsilon RII/**CD23**) in human B cells by increasing the extent of its cleavage. Bourget I; Di Berardino W; Breittmayer J P; Grenier-Brossette N; Plana-Prades M; **Bonnefoy J Y**; Cousin J L. (Laboratoire d'Immunologie Cellulaire et

Moleculaire INSERM U364, Faculte de Medecine, Pasteur, Nice, France.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 Jul) 25 (7) 1872-6. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB CD20 monoclonal **antibody** (mAb) B1 is known to inhibit B cell proliferation. We show that B1 reduced both anti-mu + interleukin-4 (IL-4)-induced DNA synthesis and the concomitant expression of **CD23** at the surface of human tonsillar B cells. B1 mAb had no effect on **CD23** mRNA levels. The disappearance of **CD23** molecule from the surface correlates with an increase of soluble **CD23** fragments in the culture medium, indicating that CD20 mAb B1 stimulated the cleavage of the molecule. B1 also inhibits IgE production by peripheral blood mononuclear cells cultured in the presence of IL-4. Suppression of IgE synthesis and enhancement of **CD23** cleavage are concomitant but appear not to be functionally related.

L84 ANSWER 11 OF 36 MEDLINE DUPLICATE 6

96071560 Document Number: 96071560. PubMed ID: 7585180. Marked amelioration of established collagen-induced arthritis by treatment with **antibodies** to **CD23** in vivo. Plater-Zyberk C; **Bonnefoy J Y.** (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland.) NATURE MEDICINE, (1995 Aug) 1 (8) 781-5. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB **CD23** is a low-**affinity** receptor for immunoglobulin E (IgE) expressed by a variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. **CD23** regulates many functional aspects of immune cells, both in its cell-associated and soluble forms. In view of the increased levels of **CD23** in rheumatoid arthritis, we have studied the effect of neutralizing **CD23** in type II collagen-induced arthritis in mice, a model for human rheumatoid arthritis. Successful disease modulation is achieved by treatment of arthritic DBA/1 mice with either polyclonal or monoclonal **antibodies** to mouse **CD23**. Treated mice show a dose-related amelioration of arthritis with significantly reduced clinical scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decrease in cellular infiltration of the synovial sublining layer and limited destruction of cartilage and bone is evident in animals treated with therapeutic doses of anti-**CD23 antibody**. These findings demonstrate the involvement of **CD23** in a mouse model of human rheumatoid arthritis.

L84 ANSWER 12 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)

95:512899 The Genuine Article (R) Number: RK868. **CD23** REGULATES MONOCYTE ACTIVATION THROUGH A NOVEL INTERACTION WITH THE ADHESION MOLECULES CD11B-CD18 AND CD11C-CD18. LECOANETHENCHOZ S (Reprint); GAUCHAT J F; AUBRY J P; GRABER P; LIFE P; PAULEUGENE N; FERRUA B; CORBI A L; DUGAS B; PLATERZYBERK C; **BONNEFOY J Y.** GLAXO INST MOLEC BIOL SA, CHEM AULX 14, CH-1228 GENEVA, SWITZERLAND (Reprint); HOP KREMLIN BICETRE, NEUROIMMUNOL LAB, F-94320 LE KREMLIN BICETRE, FRANCE; FAC MED NICE, PHARMACOL LAB, F-06107 NICE, FRANCE; HOSP PRINCESA, E-28006 MADRID, SPAIN; HOP LA PITIE SALPETRIERE, IMMUNOHEMATOL LAB, CNRS, URA 625, F-75013 PARIS, FRANCE. IMMUNITY (JUL 1995) Vol. 3, No. 1, pp. 119-125. ISSN: 1074-7613. Pub. country: SWITZERLAND; FRANCE; SPAIN. Language: ENGLISH. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB **CD23** is expressed on a variety of haemopoietic cells and displays pleiotropic activities in vitro. We report that in addition to CD21 and IgE, **CD23** interacts specifically with the CD11b and CD11c, the alpha chains of the beta 2 integrin adhesion molecule complexes CD11b-CD18 and CD11c-CD18, on monocytes. Full-length recombinant **CD23** incorporated into fluorescent liposomes was shown to bind to

COS cells transfected with cDNA encoding either CD11b-CD18 or CD11c-CD18 but not with CD11a-CD18, The interactio n was specifically inhibited by anti-CD11b or anti-CD11c, respectively, and by anti-**CD23** MAbs. The functional significance of this ligand pairing was demonstrated by triggering CD11b and CD11e on monocytes with either recombinant **CD23** or anti-CD11b and anti-CD11c MAbs to cause a marked increase in nitrite-oxidative products and proinflammatory cytokines (IL-1 beta, IL-6, and TNF alpha). These **CD23**-mediated activities were decreased by Fab fragments of MAbs to CD11b, CD11c, and **CD23**. These results demonstrate that CD11b and CD11c are receptors for **CD23** and that this novel ligand pairing regulates important activities of monocytes.

L84 ANSWER 13 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)
95:536491 The Genuine Article (R) Number: RM261. REGULATION OF IGE SYNTHESIS BY **CD23**/CD21 INTERACTION. **BONNEFOY J Y (Reprint)**; GAUCHAT J F; LIFE P; GRABER P; AUBRY J P; LECOANETHENCHOZ S. GLAXO INST MOLEC BIOL, DEPT IMMUNOL, 14 CHEMIN AUIX, CH-1228 PLAN LES OUATES, SWITZERLAND (Reprint); GLAXO INST MOLEC BIOL, GENEVA, SWITZERLAND. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (MAY/JUL 1995) Vol. 107, No. 1-3, pp. 40-42. ISSN: 1018-2438. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB At least two cell-derived signals have been shown to be necessary for the induction of immunoglobulin isotype switching in B cells. The first signal is given by either of the soluble lymphokines interleukin (IL)-4 or IL-13 which induce germline epsilon transcript expression, but alone is insufficient to trigger secretion of IgE. The second signal is provided by a physical interaction between B cells and activated T cells, basophils and mast cells, and it has been shown that the CD40/ CD40L pairing is crucial for mediating lgE synthesis. In HIGM1 syndrome, which is characterised by greatly decreased levels of IgG, IgA and IgE, there are mutations in CD40L resulting in a completely non-functional extracellular domain. CD40L is therefore playing a central role in Ig switching. Amongst the numerous pairs of surface adhesion molecules, the **CD23**/CD21 pair seems to play a key role in the generation of IgE. The **CD23** molecule is positively and negatively regulated by factors which increase or decrease IgE production, re- spectively. **Antibodies** to **CD23** have been shown to inhibit IL-4-induced human IgE production in vitro and to inhibit antigen-specific IgE responses in a rat model, in an isotype-selective manner. **CD23** interacts with CD21 on B cells, preferentially driving IgE production. **CD23** recognises two main epitopes on the CD21 molecule. One region consists of short consensus repeat sequences (SORs) 1-2 and the other of SCRs 5-8. In the latter region ASn370 and Asn295 are critical in the interaction with the lectin **CD23**. Therefore, a restricted number of cytokines and surface molecules seems to selectively regulate human IgE synthesis.

L84 ANSWER 14 OF 36 MEDLINE DUPLICATE 7
94165096 Document Number: 94165096. PubMed ID: 7509812. CD20 monoclonal **antibodies** stimulate extracellular cleavage of the low **affinity** receptor for IgE (Fc epsilon RII/**CD23**) in Epstein-Barr-transformed B cells. Bourget I; Di Berardino W; Breittmayer J P; Grenier-Brossette N; Plana-Prades M; **Bonnefoy J Y**; Cousin J L. (Laboratoire d'Immunologie Cellulaire et Moleculaire, Institut National de la Sante et de la Recherche Medicale (INSERM) U364, Nice, France.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Mar 4) 269 (9) 6927-30. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.
AB This study demonstrates that monoclonal **antibodies** to the B cell-specific CD20 molecule down-regulate both constitutive and interleukin-4-induced **CD23** expression on Epstein-Barr-transformed B cells. This effect of CD20 **antibody** B1 does not

take place at the transcriptional level as shown by the lack of effect on the **CD23** mRNA level. Incorporation of 35S-labeled amino acids into **CD23** polypeptide chain is not affected either. In cycloheximide-treated cells, B1 increases the decline of **CD23** from the cell surface. The disappearance of **CD23** molecule correlates with an increase of soluble **CD23** fragments detected in the culture medium. Taken collectively, these results indicate that CD20 mAb B1 stimulates the cleavage of the **CD23** molecule at the surface of B cells.

L84 ANSWER 15 OF 36 MEDLINE DUPLICATE 8
94267186 Document Number: 94267186. PubMed ID: 7515913. **CD23** interacts with a new functional extracytoplasmic domain involving N-linked oligosaccharides on CD21. Aubry J P; Pochon S; Gauchat J F; Nueda-Marin A; Holers V M; Graber P; Siegfried C; **Bonnefoy J Y**. (Glaxo Institute for Molecular Biology, Geneva, Switzerland.) JOURNAL OF IMMUNOLOGY, (1994 Jun 15) 152 (12) 5806-13. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Human CD21 has been described as a receptor for the C3d,g and iC3b proteins of complement, for the Epstein-Barr virus, and also for IFN-alpha. We reported recently that **CD23**, a low **affinity** receptor for IgE (Fc epsilon R2), is a new functional ligand for CD21. To determine the site of interaction of **CD23** on CD21, we analyzed the ability of purified recombinant **CD23** incorporated into fluorescent liposomes to bind CD21 mutants bearing various deletions of extracytoplasmic short consensus repeats (SCRs). We found that the site of interaction of **CD23** on CD21 is on SCRs 5 to 8, with contribution of SCRs 1 and 2. Tunicamycin treatment of CD21-transfected K562 cells strongly inhibited the binding of **CD23** -liposomes, suggesting that an N-linked sugar, present on SCRs 5 to 8, is involved in the **CD23**/CD21 interaction. By mutating together or individually, the three asparagines present on SCRs 5 to 8, asparagines (Asn) 370 and 295, but not Asn 492, were shown to be involved critically in the binding of **CD23**. Furthermore, we mapped the binding sites of a panel of anti-CD21 mAbs and found that at least six epitopes can be detected on CD21. The mAbs that inhibit the most **CD23** binding to CD21 map in SCRs 5 to 8. This study indicates that SCRs 5 to 8 represent a novel functional domain on the CD21 molecule, and is the first demonstration of an activity of an extracytoplasmic region of the CD21 outside of SCRs 1 to 4.

L84 ANSWER 16 OF 36 MEDLINE DUPLICATE 9
95104280 Document Number: 95104280. PubMed ID: 7805725. **CD23** /CD21 interaction is required for presentation of soluble protein antigen by lymphoblastoid B cell lines to specific CD4+ T cell clones. Grosjean I; Lachaux A; Bella C; Aubry J P; **Bonnefoy J Y**; Kaiserlian D. (Inserm U404 Immunite et Vaccination, Institut Pasteur de Lyon, France.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1994 Dec) 24 (12) 2982-6. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Previous studies have documented a role for membrane-bound **CD23** (the low **affinity** Fc epsilon RII) in presentation of alloantigens by B cells. The aim of the present study was to examine the involvement of cell surface **CD23** in presentation of more conventional soluble protein antigens to T cells. We show that **antibodies** to **CD23** and to its lymphocyte-associated second ligand, CD21, inhibit presentation of the cow's milk allergen casein, by autologous **CD23**+CD21+ B-EBV cell lines to casein-specific HLA-DP-restricted CD4+ T cell clones obtained from patients with either reaginic or enterophatic forms of cow's milk protein intolerance. Maximal inhibition was achieved when the **antibodies** were added at the initiation of the culture. The absence of specific inhibition by an anti-DR alpha monoclonal **antibody** (mAb) argues

against a steric hindrance phenomenon impeding access of the T cell receptor to major histocompatibility complex class II molecules. Rather, anti-**CD23** and anti-CD21 mAb-induced inhibition of antigen presentation seems to affect at least partly, heterotypic conjugate formation through **CD23**/CD21 interaction. Double immunofluorescence labeling of the T cell clones and **antibody** inhibition of T/B conjugate formation shows that functional **CD23** and CD21 molecules are induced on T cells following contact with B-EBV cell lines. Taken together, these data indicate that **CD23**/CD21 interactions between T and B cells are required for presentation of soluble protein antigens by B-EBV cell lines to specific CD4+ T cells. The potential implications of these findings for allergen-specific T cell activation are discussed.

L84 ANSWER 17 OF 36 MEDLINE DUPLICATE 10
94208860 Document Number: 94208860. PubMed ID: 7512529. Stimulation of human IgE production by a subset of anti-CD21 monoclonal **antibodies**: requirement of a co-signal to modulate epsilon transcripts. Henchoz S; Gauchat J F; Aubry J P; Graber P; Pochon S; **Bonnefoy J Y**. (Glaxo Institute for Molecular Biology, Geneva, Switzerland.) IMMUNOLOGY, (1994 Feb) 81 (2) 285-90. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD21, the receptor for Epstein-Barr virus (EBV) and the complement receptor-2 (CR2), was recently found to interact specifically with **CD23**, a low-**affinity** receptor for IgE, and to regulate IgE production. Therefore, the effect of different anti-CD21 monoclonal **antibodies** (mAb) on IgE synthesis by blood mononuclear cells was investigated. One anti-CD21 mAb, BU-33, was able to increase significantly (more than threefold) interleukin-4 (IL-4)-induced IgE synthesis, whereas HB-5, OKB-7 and B2 anti-CD21 mAb had no effect. BU-33 had no effect on IgG and IgA production and produced only a moderate increase in IgM production. Recombinant, 29,000 MW, soluble **CD23** (sCD23) expressed in COS cells exhibited the same IgE-enhancing activity. BU-33 was the best inhibitor of **CD23**-liposome binding to the CD21-positive cell line RPMI-8226 when compared to the other anti-CD21 mAb tested. BU-33 identified a different epitope on CD21. The effect of BU-33 on IgE production by purified tonsillar B cells and highly purified germinal centre B cells, was dependent on the presence of T cells or anti-CD40 mAb stimulation. Molecular analysis revealed that BU-33 alone failed to induce germline epsilon mRNA but increased the IL-4-induced germline epsilon transcription levels. Moreover, BU-33 had a synergistic effect on anti-CD40 mAb or T-cell-induced productive epsilon transcript expression. These results therefore indicate that the **CD23**-CD21 interaction needs a co-signal for B-cell differentiation towards IgE production.

L84 ANSWER 18 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)
93:665248 The Genuine Article (R) Number: MD626. CD21 EXPRESSED ON BASOPHILIC CELLS IS INVOLVED IN HISTAMINE-RELEASE TRIGGERED BY **CD23** AND ANTI-CD21 **ANTIBODIES**. BACON K; GAUCHAT J F; AUBRY J P; POCHON S; GRABER P; HENCHOZ S; **BONNEFOY J Y (Reprint)**. GLAXO INST MOLEC BIOL, IMMUNOL SECT, 14 CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND. EUROPEAN JOURNAL OF IMMUNOLOGY (OCT 1993) Vol. 23, No. 10, pp. 2721-2724. ISSN: 0014-2980. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recombinant full-length human **CD23** incorporated into fluorescent liposomes was used to detect a ligand for **CD23** on the basophilic leukemia cell line, KU 812. Based on our recent finding that **CD23** interacts with CD21 on subsets of B and T cells, we investigated if the same ligand was involved on KU 812 cells. An anti-CD21 monoclonal **antibody** (mAb) BU-33, was able to totally block **CD23**-liposome binding to KU 812 cells. Moreover, KU 812 cells

express CD21 mRNA and have a cell surface molecule that reacts with anti-CD21 mAb. The **CD23**/CD21 interaction was not merely physical but was also associated with an increase in histamine release by KU 812 cells. Both recombinant soluble **CD23** and an anti-CD21 mAb increased histamine release by KU 812 cells. The **CD23** and anti-CD21 mAb-mediated effect on histamine release was not restricted to the leukemic cell line, but was also observed with normal human blood basophils. These data demonstrate that CD21 is expressed on basophilic cells and that CD21 controls histamine production upon ligand-induced stimulation (**CD23** or anti-CD21 mAb).

L84 ANSWER 19 OF 36 MEDLINE

93314717 Document Number: 93314717. PubMed ID: 7686859. Interleukin-9 potentiates the interleukin-4-induced immunoglobulin (IgG, IgM and IgE) production by normal human B lymphocytes. Dugas B; Renauld J C; Pene J; **Bonnefoy J Y**; Peti-Frere C; Braquet P; Bousquet J; Van Snick J; Mencia-Huerta J M. (INSERM/CJF 92-10, Hopital Arnaud de Villeneuve, Montpellier, France.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 Jul) 23 (7) 1687-92. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB IgE production by normal peripheral blood lymphocytes (PBL) is known to be triggered upon stimulation by interleukin (IL)-4. In the present study we showed that IL-9, another T cell-derived cytokine, markedly potentiated IgE production induced by suboptimal doses of IL-4, whereas no effect of IL-9 was observed in the absence of IL-4. The potentiating effect of IL-9 appeared to be associated with the increased frequency of IgE-producing cells, as revealed by a specific ELISA-spot assay. Under the same experimental conditions, IL-9 also enhanced the IL-4-induced IgG production but did not elicit IgM production. However, IL-9 did not amplify the IL-4-dependent expression of membrane-bound and soluble low **affinity** receptor for IgE (**CD23**). IL-4-induced IgE production was also potentiated by IL-6 but not by tumor necrosis factor-alpha and IL-1 beta. The possibility that the activity of IL-9 was mediated by IL-6 released from accessory cells was excluded by the observations that monocyte depletion did not abolish the effect of IL-9 and that IL-9 was still active on fluorescence-assisted cell sorted CD20+ B lymphocytes co-cultured with irradiated murine EL4 cells. In addition, IL-9 was shown to potentiate the IL-4-induced IgG and IgM production by normal human B lymphocytes preactivated with Staphylococcus aureus Cowan strain. Taken together, these data suggest that IL-9 plays a regulatory role in the IL-4-dependent immunoglobulin production.

L84 ANSWER 20 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 11

93300876 EMBASE Document No.: 1993300876. Inhibition of an in vivo antigen-specific IgE response by **antibodies** to **CD23**. Flores-Romo L.; Shields J.; Humbert Y.; Graber P.; Aubry J.-P.; Gauchat - J.F.; Ayala G.; Allet B.; Chavez M.; Bazin H.; Capron M.; **Bonnefoy J.-Y.**. Glaxo Inst. for Molecular Biology, CP 674,CH-1228 Geneva, Switzerland. Science 261/5124 (1038-1041) 1993. ISSN: 0036-8075. CODEN: SCIEAS. Pub. Country: United States. Language: English. Summary Language: English.

AB Immunoglobulin E (IgE) mediates many allergic responses. **CD23** is a 45- kilodalton type II transmembrane glycoprotein expressed in many cell types. It is a low-**affinity** IgE receptor and interacts specifically with CD21, thereby modulating IgE production by B lymphocytes in vitro. In an in vivo model of an allergen-specific IgE response, administration of a rabbit polyclonal **antibody** to recombinant human truncated **CD23** resulted in up to 90 percent inhibition of ovalbumin-specific IgE synthesis. Both Fabs and intact IgG inhibited IgE production in vitro and in vivo. Thus, **CD23** participates in the regulation of IgE synthesis in vivo and so could be important in allergic disease.

L84 ANSWER 21 OF 36 MEDLINE DUPLICATE 12

93209301 Document Number: 93209301. PubMed ID: 8458382. A subset of anti-CD21 **antibodies** promote the rescue of germinal center B cells from apoptosis. **Bonnefoy J Y**; Henchoz S; Hardie D; Holder M J; Gordon J. (Immunology Section, Glaxo Institute for Molecular Biology, Plan-les-Ouates/Geneva, Switzerland.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 Apr) 23 (4) 969-72. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Germinal center cells (GCC) are programmed to die by apoptosis unless they receive a positive signal for rescue. The primary signal in vivo is believed to be dependent on interaction with antigen held as immune complexes on follicular dendritic cells (FDC), a subset of which express large amounts of **CD23**, a low-**affinity** receptor for IgE. Recombinant soluble **CD23** (sCD23) and interleukin-1 have been found to potentiate the survival of GCC in vitro. Recently, **CD23** was shown to interact specifically with a ligand other than IgE, namely CD21 (CR2/Epstein-Barr virus receptor). In the present study, we show that a subset of anti-CD21 monoclonal **antibodies** behave similarly to soluble **CD23** in their effect on GCC inasmuch as they: (i) diminish the occurrence of apoptosis; (ii) promote a plasmacytoid appearance in rescued cells; (iii) up-regulate expression of the Bcl-2 proto-oncogene. These findings indicate that FDC-derived **CD23** exerts its effects on GCC via CD21.

L84 ANSWER 22 OF 36 MEDLINE DUPLICATE 13

93187384 Document Number: 93187384. PubMed ID: 8095276. A multiparameter flow cytometric method to study surface molecules involved in interactions between subpopulations of cells. Aubry J P; Shields J G; Jansen K U; **Bonnefoy J Y**. (Glaxo Institute for Molecular Biology S.A., Geneva, Switzerland.) JOURNAL OF IMMUNOLOGICAL METHODS, (1993 Feb 26) 159 (1-2) 161-71. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB The interactions between T and B lymphocytes are mediated by several antigen-independent adhesion molecules including LFA-1/ICAM-1 and CD2/LFA-3. Recently new pairs of adhesion molecules involved in T and B interactions have been described: CD28/B7, CD5/CD72 and CD45RO/CD22. In order to study these heterotypic adhesion events, the phenotypes of the subpopulations as well as new potential adhesion molecules involved in conjugate formation, we have developed a flow cytometric method which analyses conjugate formation between T and B cells. The two types of cells were loaded with two vital intracellular dyes: human T lymphocytes purified from blood or tonsils were labelled with BCECF-AM (green fluorescence) and the B lymphoblastoid cell line, RPMI 8866 was labelled with Indo-1-AM (blue fluorescence). The two labelled cell populations were mixed, gently centrifuged for 5 min and then incubated at 37 degrees C in a waterbath for 5 min. The cells were then gently resuspended by inversion and analysed with a double laser flow cytometer. This method permitted us to discover new molecular interactions since preincubation of the two populations with monoclonal **antibodies** directed against some surface molecules inhibited conjugate formation. As an example, using this technique we found that the low **affinity** IgE receptor, **CD23** and the CR2/EBV receptor are involved in T cell/B cell adhesion and can therefore be considered as a new pair of adhesion molecules. This method also seems to be applicable to recombinant cells bearing a single adhesion molecule such as LFA-1 and ICAM-1. A particular advantage of the two intracellular dyes we used is that they are compatible with the dyes commonly used for classical simultaneous triple colour immunofluorescence (phycoerythrin and Cy-Chrome). We were thus able to determine the subpopulations involved in forming conjugates and we found that T-B conjugates were preferentially formed by CD4, CD45RO positive T cells, which are believed to be the memory T lymphocytes.

L84 ANSWER 23 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)

93:562468 The Genuine Article (R) Number: LW675. INTESTINAL EPITHELIAL-CELLS EXPRESS THE **CD23**/FC-EPSILON-RII MOLECULE - ENHANCED EXPRESSION IN ENTEROPATHIES. KAISERLIAN D (Reprint); LACHAUX A; GROSJEAN I; GRABER P; **BONNEFOY J Y**. INST PASTEUR, UNITE IMMUNOL & STRATEGIE VACCINALE, AVE TONY GARNIER, F-69365 LYON 07, FRANCE (Reprint); GLAXO INST MOLEC BIOL, GENEVA, SWITZERLAND; HOP EDOUARD HERRIOT, SERV HEPATOGASTROENTEROL INFANTILE, F-69374 LYON 08, FRANCE. IMMUNOLOGY (SEP 1993) Vol. 80, No. 1, pp. 90-95. ISSN: 0019-2805. Pub. country: FRANCE; SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Immunohistochemical analysis of normal human intestine revealed that two anti-**CD23** monoclonal **antibodies** (mAb), EBVCS 1 and EBVCS 2, reacted with human intestinal epithelial cells. Both mAb exhibited an exclusive reactivity with epithelial cells of the small and large bowels. Staining with both EBVCS 1 and EBVCS 2 was localized on the apical and basal sides of enterocytes. Enhanced expression of **CD23** on gut epithelial cells was found in inflammatory bowel diseases, in children with food intolerance to cows' milk proteins and in a young infant with severe autoimmune enteropathy. Western blot analysis of anti-**CD23** mAb reactivity with gut epithelial cell extracts showed the presence of a non-reducible 42,000-45,000 M(r) polypeptide compatible with the membrane form of the intact **CD23** molecule. These data show that **CD23** is constitutively expressed by intestinal epithelial cells and that its expression is enhanced in enteropathies.

L84 ANSWER 24 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)
93:64740 The Genuine Article (R) Number: KJ589. A NEW PAIR OF SURFACE MOLECULES INVOLVED IN HUMAN IGE REGULATION. **BONNEFOY J Y (Reprint)**; POCHON S; AUBRY J P; GRABER P; GAUCHAT J F; JANSEN K; FLORESROMO L. GLAXO INST MOLEC BIOL, 14 CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND (Reprint). IMMUNOLOGY TODAY (JAN 1993) Vol. 14, No. 1, pp. 1-2. ISSN: 0167-4919. Pub. country: SWITZERLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The molecules controlling IgE production are the subject of intense study in the effort to find new ways to treat allergic diseases. One candidate, the **CD23** molecule, a low **affinity** receptor for IgE, was recently identified to interact with another molecule, named CD21, in the regulation of IgE production.

L84 ANSWER 25 OF 36 MEDLINE DUPLICATE 14
92289818 Document Number: 92289818. PubMed ID: 1534760. Spontaneous and ligand-induced endocytosis of **CD23** (Fc epsilon receptor II) from the surface of B lymphocytes generates a 16-kDa intracellular fragment. Grenier-Brossette N; Bourget I; Akoundi C; **Bonnefoy J Y**; Cousin J L. (INSERM U210, Faculte de Medecine (Pasteur), Nice, France.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1992 Jun) 22 (6) 1573-7. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB It has been reported that the 45-kDa low-**affinity** Fc epsilon receptor (Fc epsilon RII) on B cells is cleaved spontaneously from the cell surface to release soluble fragments. This study demonstrates an additional fate of the Fc epsilon RII. 125I-labeled **CD23**+ B cells were cultured for 24 h at 37 degrees C. After lysis, cell extracts were immunoprecipitated with **CD23** monoclonal **antibodies** . Using this methodology, we demonstrated that an increasing amount of the labeled Fc epsilon RII becomes progressively resistant to externally applied trypsin, indicating that a fraction of the cell surface receptors are internalized. In parallel, a labeled 16-kDa material, recognized by **CD23** monoclonal **antibodies** directed to the lectin-like domain of the Fc epsilon-RII appears inside the cells. Chloroquine does not affect internalization of the Fc epsilon RII, but completely abolishes the formation of the intracellular fragment, suggesting that the receptor is processed by proteolytic cleavage in acidic organelle. In addition,

the internalization is enhanced in the presence of **CD23** monoclonal **antibodies**. These data demonstrate that Fc epsilon RII can be internalized by ligand-induced endocytosis and subsequently cleaved in an intracellular compartment. These results also support the view that the Fc epsilon RII is involved in antigen focusing and antigen presentation.

L84 ANSWER 26 OF 36 MEDLINE DUPLICATE 15
92350302 Document Number: 92350302. PubMed ID: 1386409. CD21 is a ligand for **CD23** and regulates IgE production. Aubry J P; Pochon S; Graber P; Jansen K U; **Bonnefoy J Y**. (Glaxo Institute for Molecular Biology, Geneva, Switzerland.) NATURE, (1992 Aug 6) 358 (6386) 505-7. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The molecule **CD23**, a low-**affinity** receptor for IgE (Fc epsilon R2), is a type II transmembrane molecule expressed on many haemopoietic cell types. **CD23** has pleiotropic roles in the control of lymphocyte behaviour, suggesting that **CD23** may interact with another ligand in addition to IgE. To identify such a **CD23** ligand, we expressed and purified full-length recombinant **CD23**, incorporated it into fluorescent liposomes and used these as a probe. We report here that fluorescent liposomes carrying **CD23** interact specifically with the cell-surface protein CD21, identified as the receptor for Epstein-Barr virus and the complement receptor-2 on B cells, some T cells and follicular dendritic cells. In addition, fluorescent **CD23**-liposomes were shown to bind to hamster kidney cells (BHK-21) transfected with CD21 complementary DNA. The interaction between fluorescent **CD23**-liposomes and B cells or CD21-transfected BHK-21 cells was specifically inhibited by anti-CD21 and anti-**CD23** monoclonal **antibodies**. Western blotting analysis revealed that 14C-labelled liposomes carrying **CD23**, in contrast to anti-CD21 **antibodies**, reacted with a subtype of CD21 molecules. Triggering of CD21 either with an anti-CD21 **antibody** or with recombinant soluble **CD23** was shown to increase specifically interleukin-4-induced IgE production from blood mononuclear cells. These results demonstrate that the cell-surface protein CD21 is a ligand for **CD23** and that the pairing of these molecules may participate in the control of IgE production.

L84 ANSWER 27 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R)
92:419969 The Genuine Article (R) Number: JC566. THE ROLE OF **CD23** AND ITS RECEPTOR IN T-CELL B-CELL INTERACTION - IMPLICATIONS FOR REGULATION OF IGE SYNTHESIS. SHIELDS J; POCHON S; AUBRY J P; FLORESROMO L; JANSEN K; GRABER P; **BONNEFOY J Y (Reprint)**. GLAXO INST MOLEC BIOL, CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND. RESEARCH IN IMMUNOLOGY (MAY 1992) Vol. 143, No. 4, pp. 425-427. ISSN: 0923-2494. Pub. country: SWITZERLAND. Language: ENGLISH.

L84 ANSWER 28 OF 36 MEDLINE DUPLICATE 16
92364541 Document Number: 92364541. PubMed ID: 1386872. Demonstration of a second ligand for the low **affinity** receptor for immunoglobulin E (**CD23**) using recombinant **CD23** reconstituted into fluorescent liposomes. Pochon S; Graber P; Yeager M; Jansen K; Bernard A R; Aubry J P; **Bonnefoy J Y**. (Glaxo Institute for Molecular Biology, Plan-Les-Ouates, Geneva, Switzerland.) JOURNAL OF EXPERIMENTAL MEDICINE, (1992 Aug 1) 176 (2) 389-97. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Recombinant full-length human **CD23** has been incorporated into fluorescent liposomes to demonstrate the existence of a ligand for **CD23** that is different from the previously known ligand, immunoglobulin E (IgE). The novel ligand for **CD23** is expressed on subsets of normal T cells and B cells as well as on some myeloma cell lines. The interaction of full-length **CD23** with its ligand is

specifically inhibited by anti-**CD23** monoclonal **antibodies** and by IgE, and it is Ca2+ dependent. Moreover, tunicamycin treatment of a **CD23**-binding cell line, RPMI 8226, significantly reduced the binding of **CD23** incorporated into fluorescent liposomes, and a sugar, fucose-1-phosphate, was found to inhibit **CD23**-liposome binding to RPMI 8226 cells, suggesting the contribution of sugar structures on the **CD23** ligand. In addition, **CD23**-transfected COS cells were shown to form specific conjugates with the cell line RPMI 8226. These data demonstrate that **CD23** interacts with a ligand, which is different from IgE, and that **CD23** can be considered as a new surface adhesion molecule involved in cell-cell interactions.

L84 ANSWER 29 OF 36 MEDLINE DUPLICATE 17
92276826 Document Number: 92276826. PubMed ID: 1534340. Purification and characterization of biologically active human recombinant 37 kDa soluble **CD23** (sFc epsilon RII) expressed in insect cells. Graber P; Jansen K; Pochon S; Shields J; Aubonney N; Turcatti G; **Bonnefoy J Y.** (Glaxo Institute for Molecular Biology S.A., Geneva, Switzerland.) JOURNAL OF IMMUNOLOGICAL METHODS, (1992 May 18) 149 (2) 215-26. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Human recombinant soluble 37 kDa **CD23** has been expressed in insect cells and secreted into the culture medium using the IL-2 leader sequence. The 37 kDa **CD23** was purified 600-fold to homogeneity by monoclonal **antibody affinity** chromatography and gel filtration. The pure protein is monomeric, glycosylated, depleted of one N terminal amino acid and contains four disulphide bonds. It degrades into smaller fragments of 33, 29 and 25 kDa if purified in the absence of protease inhibitors. The same pattern of proteolytic fragments is observed when the pure preparation is incubated at room temperature for 3 weeks. Physical characterization of the 37 kDa **CD23** by circular dichroism indicates that the protein contains mainly beta sheet and 20% of alpha helical structures. Specific binding of IgE to natural **CD23** (low **affinity** IgE receptor) was inhibited by purified recombinant 37 kDa **CD23**. Moreover, purified recombinant 37kDa **CD23** and interleukin-1 promoted the survival of germinal centre B cells.

L84 ANSWER 30 OF 36 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 18
91:364397 The Genuine Article (R) Number: FT273. IGE AND SWITCHING PHENOMENA. **BONNEFOY J Y (Reprint)**. GLAXO INST MOLEC BIOL, CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND (Reprint). SEMAINE DES HOPITAUX (1991) Vol. 67, No. 26-2, pp. 1199-1200. Pub. country: SWITZERLAND. Language: French.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In allergic disorders, IgE increases following allergen stimulation. In vitro IgE synthesis is the result of a complex interaction between T-cells, B-cells and monocytes, controlled by cytokines produced by T-cells and monocytes (IL-4, IL-5, IFN-gamma, and IL-6). IL-4 acts as a switching factor to induce synthesis of IgE. IFN-gamma inhibits IL-4 induced IgE synthesis. IL-4 is a mastocyte growth factor, as well as IL-3. Moreover, IL-4 is a potent inducer of FceR/**CD23** expression of B-cells and monocytes. Monoclonal anti-**CD23** **antibodies** inhibit IL-4-induced IgE synthesis in an isotype-specific manner. IL-4-producing T-cells also produce IL-5 which induces differentiation of eosinophil precursors. Eosinophils, in turn, express low **affinity** receptors for IgE when activated. Activation of the IgE system thus leads to increased IgE production and increased expression of IgE receptors. This results in increased receptor-ligand interactions, resulting in release of numerous chemical mediators involved in the pathogenesis of allergic disorders.

L84 ANSWER 31 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 19
91341164 EMBASE Document No.: 1991341164. Expression of human recombinant **CD23** in insect cells. Jansen K.U.; Shields J.; Gordon J.; Cairns J.; Graber P.; **Bonnefoy J.-Y.**. Glaxo Institute for Molecular Biology S.A. 46 route des Acacias, 1211 Geneva 24, Switzerland. Journal of Receptor Research 11/1-4 (507-520) 1991.
ISSN: 0197-5110. CODEN: JRERDM. Pub. Country: United States. Language: English. Summary Language: English.

AB Human **CD23** (low **affinity** receptor for IgE) has been expressed in insect cells (Sf9) using the baculovirus expression system and the baculovirus transfer vector pAc373. Insect cells infected with a recombinant baculovirus coding for **CD23** synthesized a polypeptide not found in wild-type infected insect cells that had antigenic properties similar to natural **CD23** produced in RPMI 8866 cells. Surface expression of recombinant **CD23** was demonstrated by its ability to bind IgE. Recombinant **CD23** expressed in insect cells had a slightly lower molecular weight (43 kDa) than that of natural **CD23** (45 kDa) from RPMI 8866 cells as detected by SDS-PAGE followed by Western-blotting. **Affinity** -purified recombinant **CD23** from infected insect cells showed B-cell growth promoting activity. These observations demonstrate for the first time that biologically active recombinant **CD23** can be produced by the baculovirus expression system, thus providing a useful source of recombinant material to elucidate the biological functions of **CD23**.

L84 ANSWER 32 OF 36 MEDLINE
91291729 Document Number: 91291729. PubMed ID: 1829628. Mononuclear cell-bound **CD23** is elevated in both atopic dermatitis and psoriasis. Muller K M; Rocken M; Joel D; **Bonnefoy J Y**; Saurat J H; Hauser C. (Department of Dermatology, Hopital Cantonal Universitaire, Geneva, Switzerland.) JOURNAL OF DERMATOLOGICAL SCIENCE, (1991 Mar) 2 (2) 125-33. Journal code: 9011485. ISSN: 0923-1811. Pub. country: Netherlands. Language: English.

AB As patients with atopic dermatitis (AD) frequently have elevated serum IgE levels, the relation of this disease to **CD23**/Fc epsilon RII, a low **affinity** Fc receptor for IgE, and its soluble forms, sCD23, was studied. We examined the expression of **CD23** on peripheral blood mononuclear cells (PBMC) as well as the serum IgE and sCD23 levels in 33 patients with AD and in 9 patients with psoriasis in comparison with 10 healthy donors. In AD patients, the numbers of **CD23**+ unfractionated PBMC and **CD23**+ small adherent cells were significantly elevated (P less than 0.05, resp. P less than 0.005). In psoriatic patients however, **CD23** was also significantly elevated on PBMC (P less than 0.05) and on small adherent cells (P less than 0.05). There was no significant difference in the frequencies of **CD23**+ cells between AD and psoriasis patients. In all donors, **CD23** could be detected only on B cells, but not on monocytes/macrophages. In AD patients who were examined twice, an increase or decrease of the clinical AD score was always accompanied by an increase or decrease, resp., of cell-bound **CD23**. The serum sCD23 level was not significantly increased in either group of patients. Our results suggest that **CD23** should be considered as a nonspecific marker for B cell activation in the context of inflammation and not as a specific marker for AD.

L84 ANSWER 33 OF 36 MEDLINE DUPLICATE 20
88320539 Document Number: 88320539. PubMed ID: 2970644. IgE production by normal human lymphocytes is induced by interleukin 4 and suppressed by interferons gamma and alpha and prostaglandin E2. Pene J; Rousset F; Briere F; Chretien I; **Bonnefoy J Y**; Spits H; Yokota T; Arai N; Arai K; Banchereau J; +. (UNICET, Laboratory for Immunological Research, Dardilly, France.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE

UNITED STATES OF AMERICA, (1988 Sep) 85 (18) 6880-4. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The effect of human recombinant interleukin 4 (IL-4) on **antibody** production by normal peripheral blood mononuclear cells enriched for B cells was investigated. IL-4 preferentially induced IgE synthesis in vitro. In addition, a low induction of IgG production was observed, whereas IL-4 had no effect on IgA and IgM synthesis. The IL-4-induced IgE production by B cells required T cells and monocytes but was specifically inhibited by an anti-IL-4 antiserum indicating that, although IL-4 acts indirectly, it is responsible for the induction of IgE synthesis. IL-4-induced IgE production was blocked in a dose-dependent way by interferon gamma (IFN-gamma), interferon alpha (IFN-alpha), and prostaglandin E2. IFN-gamma also inhibited IL-4-induced IgG production. These inhibitory effects of IFN-gamma and IFN-alpha on IgE production cannot be attributed to toxic effects since IFN-alpha induced IgM production in the presence of IL-4, whereas IFN-gamma was ineffective in inhibiting IgG production induced by IL-2. IFN-gamma, IFN-alpha, and prostaglandin E2 also inhibited IL-4-induced expression of the low-**affinity** receptor for the Fc portion of IgE (**CD23**) on B cells, indicating that there is an association between **CD23** expression and IL-4-induced IgE production.. This theory was supported by the finding that IL-4-induced IgE production was inhibited by F(ab')2 fragments of an anti-**CD23** monoclonal **antibody**.

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88089420 Document Number: 88089420. PubMed ID: 2961843. The low-**affinity** receptor for IgE (**CD23**) on B lymphocytes is spatially associated with HLA-DR antigens. **Bonnefoy J Y**; Guillot O; Spits H; Blanchard D; Ishizaka K; Banchereau J. (UNICET, Laboratory for Immunological Research, Dardilly, France.) JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Jan 1) 167 (1) 57-72. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Two hybridomas that produce the mAbs 135 and 449 B4 were obtained that inhibited the binding of IgE to the Fc epsilon RL/**CD23** on the EBV-transformed B cell line RPMI 8866. mAb 135 was obtained from a mouse immunized with RPMI 8866 cells, whereas mAb 449B4 was obtained from a mouse immunized with a partially purified preparation of Fc epsilon RL/**CD23** obtained as the eluate of an IgE immunoabsorbent loaded with a soluble extract of RPMI 8866 cells. These two mAbs bound to Fc epsilon RL/**CD23**- cell lines and precipitated two polypeptides with 36,000 Mr and 28,000 Mr, which were the HLA-DR alpha and beta chains, respectively. Immunoprecipitation with mAb 135 of NP-40 lysates from dithio-bis(succinimidyl propionate) (DSP) crosslinked 125I-labeled RPMI 8866 or normal B cells incubated with rIL-4 showed three polypeptides with 42,000, 36,000, and 28,000 Mr. The 42,000 Mr polypeptide is identical to the Fc epsilon RL/**CD23** since it could be precipitated by the anti-Fc epsilon RL/**CD23** mAb 25 after resolubilization from the SDS-PAGE gel. Immunoprecipitations of the crosslinked cell extracts carried out with the anti-Fc epsilon RL/**CD23** mAb 25 yielded the same three polypeptides. Furthermore, when RPMI 8866 or rIL-4 preincubated normal B cells were solubilized with a digitonin buffer, which prevents the dissociation of noncovalently linked polypeptide complexes, mAb 135 and mAb 25 precipitated complexes composed of three molecules with 42,000, 36,000, and 28,000 Mr. The well-characterized anti-HLA-DR mAb L243 was unable to block the binding of either IgE or mAb 135 to RPMI 8866 cells, although it could immunoprecipitate the complex (HLA-DR-Fc epsilon RL/**CD23**) from crosslinked cell lysates. Since mAb 135 and L243 were able to both bind the RPMI 8866 cells, it demonstrates that they bind to different epitopes of the HLA-DR complex, the mAb 135 epitope of the HLA-DR molecule being close to the IgE binding site of the Fc epsilon RL/**CD23**. These data demonstrated that the Fc epsilon RL/**CD23** and HLA-DR antigens are spatially associated on the B cell membrane.

L84 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2003 ACS
1987:421668 Document No. 107:21668 Production and characterization of a monoclonal **antibody** specific for the human lymphocyte low **affinity** receptor for IgE: CD 23 is a low **affinity** receptor for IgE. **Bonnefoy, Jean Yves**; Aubry, Jean Pierre; Peronne, Catherine; Wijdenes, John; Banchereau, Jacques (Lab. Immunol. Res., UNICET, Dardilly, 69570, Fr.). Journal of Immunology, 138(9), 2970-8 (English) 1987. CODEN: JOIMA3. ISSN: 0022-1767.

AB A monoclonal **antibody** to the low-**affinity** receptor for IgE on human lymphocytes was prepd. and characterized. Studies with this **antibody** revealed that the low-**affinity** receptor for IgE is the CD 23 antigen.

L84 ANSWER 36 OF 36 MEDLINE DUPLICATE 22
87224723 Document Number: 87224723. PubMed ID: 2953844. Human recombinant interleukin 4 induces Fc epsilon receptors (**CD23**) on normal human B lymphocytes. Defrance T; Aubry J P; Rousset F; Vanbervliet B; **Bonnefoy J Y**; Arai N; Takebe Y; Yokota T; Lee F; Arai K; +. JOURNAL OF EXPERIMENTAL MEDICINE, (1987 Jun 1) 165 (6) 1459-67. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Human rIL-4 is able to induce the expression of low-**affinity** receptors for IgE (Fc epsilon RL/**CD23**) on resting B lymphocytes, as determined by the binding of either the anti Fc epsilon RL/**CD23** -specific mAb 25 or IgE. Stimulation of B cells with insolubilized anti-IgM **antibody** increases the number of cells expressing Fc epsilon RL/**CD23** upon culturing with IL-4 and enhances the level of Fc epsilon RL/**CD23** expression on these cells. Fc epsilon RL/**CD23** induction is specific for IL-4 since IL-1 alpha, IL-2, IFN-gamma, B cell-derived B cell growth factor (BCGF), and a low-molecular-weight BCGF were ineffective. IFN-gamma strongly inhibited the induction of Fc epsilon RL/**CD23** by IL-4.

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